EXHIBIT 4

IN THE UNITED STATES DISTRICT COURT

FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA

CHARLESTON DIVISION

* * *

IN RE: DIGITEK PRODUCT LIABILITY

LITIGATION MDL NO. 1968

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Deposition of EJORN D. NELSON, PHARM.D., Witness herein, called by the Defendants for cross-examination pursuant to the Rules of Civil Procedure, taken before me, Mary Jo Stevens, a Notary Public in and for the State of Ohio, at the Doubletree Cincinnati Airport, 2826 Terminal Drive, Hebron, Kentucky, on Tuesday, the 22nd day of June, 2010, at 8:22 a.m.

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40-B, a one-page sheet, page 581, from Drugs in the Treatment of Heart Failure, was marked for purposes of identification.).....

(Thereupon, Defendants' Exhibit 89 40-C, a group of documents from MICROMEDEX Healthcare Series labeled Cardiac Glycosides, was marked for purposes of identification.).....

(Thereupon, Defendants' Exhibit 91 40-D, a group of documents from MICROMEDEX Healthcare Series labeled Digoxin, was marked for purposes of identification.).....

(Thereupon, Defendants' Exhibit 106 40-E, a one-page document entitled Response to Defense Pharmacologist Expert Report, was marked for purposes of identification.).....

APPEARANCES:

On behalf of the Plaintiffs:

Motley Rice, LLC

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On behalf of Defendants Actavis Totowa LLC, Actavis, Inc. and Actavis Elizabeth, LLC:

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On behalf of the Defendants Mylan Pharmaceuticals, Inc., Mylan, Inc., Mylan Bertek Pharmaceuticals, Inc. and UDL Laboratories, Inc.:

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* * *

EJORN D. NELSON, PHARM.D.

of lawful age, Witness herein, having been first duly cautioned and sworn, as hereinafter certified, was examined and said as follows:

CROSS-EXAMINATION

BY MR. MORIARTY:

Q. Tell us your full name.

A. Dr. Eljorn Don Nelson.

Q. As I understand it, you're not a medical doctor, correct?

A. I am a P H A R M D, Pharm.D. I have a doctor of pharmacy and fellowship from the National Institutes of Health.

Q. You don't have an M.D., as I understand it?

A. That's a fact.

Q. So do you typically go by doctor or professor?

A. I typically go by doctor. I have a diploma that was signed by Ronald Reagan in 1970 that says doctor on it.

(Thereupon, Defendants' Exhibit 41, a curriculum vitae of Ejorn Don Nelson, Pharm.D., was identified for purposes of identification.)

Q. Handing you what's been marked as

Defendants' Exhibit 41, that's a CV of yours that we were provided.

A. Yes, sir.

Q. Is it up to date?

A. Yeah. It's got cases appended to the back of it. The CV is pages one through eight. This is my federal case list (indicating).

Q. Well, on the version that's going to into the record, it's got the case list attached.

A. Well, that's not part of my CV so that's inappropriate. It ought to be a separate document.

MR. MORIARTY: Okay. So we will take those two pages off the CV and if you can mark that as 41-A, I would appreciate it.

(Pause in proceedings.)

(Thereupon, Defendants' Exhibit 41-A, a two-page document entitled Dr. Don Nelson's Case List, was marked for purposes of identification.)

Q. So 41-A is called Dr. Don Nelson's case list, correct? That's this (indicating).

A. Yes, that's my case list.

Q. And --

A. I guess it's 41-A.
Q. Yes. Two pages long?
A. It is.
Q. Of the cases on 41-A, did any of them involve digoxin?
A. I don't know. Some of these patients were probably taking digoxin. I don't know the answer to that question.
Q. Do you know whether any of the cases on 41-A were primarily about digoxin as opposed to any of these people taking it incidentally to other issues in the case?
A. I think that where there was involvement of digoxin, it would be incidental rather than primary from my recollection.
Q. Okay. Now, as I understand it, you are a professor emeritus with the University of Cincinnati; is that correct?
A. Yes, that's correct. That's not my only academic appointment. I'm also associate director of the Drug & Poison Information Center and professor of clinical pharmacology, cell biophysics in the department of pharmacology.
Q. Are you still working full-time?

A. Yes.
Q. And how much of your time is devoted to the academic work -- the academic work that you just mentioned as opposed to private consulting work in litigation?
A. Well, I have a full-time job and I do consulting when it arises. What percentage of my total work time, I don't know. Ten percent, something like that.
Q. Ten percent is litigation consulting?
A. Approximately.
Q. Under your consultantships, item number two says United States Pharmacopeia representative for the University of Cincinnati College of Medicine.
A. What page is that on?
Q. Four?
A. Yes, sir.
Q. Are you still in that position?
A. I don't know the answer to that question. The dean nominated me to do that a few years ago. I haven't had any recent correspondence with respect to that.
Q. When you were doing that activity,

what was your role?

A. Well, to offer about -- academic input to the USP. There were -- they were reviewing procedures and updating their -- the way they operate, going from paper to electronics and things like that. It was --

Q. Was that the specific role on which you were consulting?

A. Among others, yes. Um-hum.

Q. How would you describe the USP overall?

A. Well, USP --

Q. Briefly?

A. Yes, Counselor. USP is one of the old books that pharmacies have. The role of the -- the original role of the USP was to set standards for drugs. When pharmacy began, it began as an apothecary trade type of group, guild, and there were problems with drug standards. That is, when you picked up a particular medicament, you didn't know what was in it. Much of pharmacy came from pharmacognosy which is drugs of plant and mineral origin, which is a place that medicinal agents are derived from, and the problem with

those sources is that they vary. And so the USP was one of the early efforts to try to standardize the medicinal content of drugs and medicinal agents. So the purpose -- the original purpose of the USP was to define standards for drug content so when a health professional reached for a tablet or a dosage of something that there was a predictable amount of medication in that unit of dosage.

Q. And the USP has continued to be updated and continues to this day; is that correct?

A. It does.

Q. And the USP contains test methods also, does it not?

A. It contains some, yes.

Q. And what is, if you know, what is the FDA's view of the sort of authoritative nature of the USP?

A. Well, if I have -- if I'm a pharmaceutical manufacturer and I have a medication and I say there's X hundred milligrams of active ingredients in a product per dosage form, the USP defines what that specific content is and you have either got

that content in the dosage form or you don't. So the FDA's view is that a dosage form is a dosage form to USP standards. If it conforms to those standards and it is not -- if it does not conform to those standards. So if I put peanut butter in an aspirin tablet and sell it, it's not aspirin USP. It's mislabeled and misbranded because it contains something that is not supposed to be there.

Q. But not necessarily something harmful unless you have a peanut allergy, right?

MR. THOMPSON: Objection to form.

THE WITNESS: It doesn't matter whether it's harmful or not. It's something in the product that's not supposed to be there, that is not specified on the label.

Q. But the USP test methods are also the USP's standardized -- approved standardized ways to determine if the tablet has the appropriate amount of the active pharmaceutical ingredients in it, correct?

A. Yes.

Q. Am I correct that you have given hundreds of depositions?

A. Probably over a hundred. I don't have a count so I don't know the answer to that question.

Q. Do you know if it's over two hundred?

A. I don't know.

Q. Have you actually been a defendant in any lawsuits?

A. Yes.

Q. Have you been a plaintiff in any lawsuits?

A. Oh, God. I get these mailings about various class action suits that --

Q. Okay. Other than those. I don't care whether your securities dropped or your toaster burned. I mean an individual plaintiff in a case.

A. No.

Q. Now, what kind of cases -- I don't want to know about divorce or traffic ticket or things of that nature. What kind of cases have you been a defendant in?

A. I cleaned up some garbage on a property line and my neighbor sued me for cleaning up the garbage and won two thousand

dollars.

Q. Anything else?

A. No.

Q. We asked you to bring a number of materials with you to the deposition. Most of it included what you reviewed to prepare for -- to draft your report and prepare opinions in this case?

A. Yes.

Q. Is that the stack of material that you handed me when you got here?

A. It is.

Q. Is there anything else that you reviewed that you left at home or at your office?

A. No.

MR. THOMPSON: Let me interrupt just one second. Dr. Nelson has provided me with several e-mails from a person in my office, Meghan Johnson Carter. I'm happy to identify them to the degree that you need to pursue whatever relief you wish, but I'm going to assert a work product privilege on these e-mails so --

MR. MORIARTY: Well, first tell me the basis of the work product privilege when

you're communicating with an expert, briefly.

MR. THOMPSON: Well, it's simply that to the extent that she is -- well, I'm not asserting a work product privilege as it's defined by the rules.

MR. MORIARTY: So you're taking the position that e-mail correspondence --

MR. THOMPSON: To and from.

MR. MORIARTY: To and from is work product, right.

MR. THOMPSON: Right.

MR. MORIARTY: Are you taking the same position with regard to the letters sent by United States Post or FedEx?

MR. THOMPSON: I don't think I have any of those so I have no position on that today.

MR. MORIARTY: Okay. So identify the e-mails by date or who is on the to/from line.

MR. THOMPSON: Okay.

MR. MORIARTY: I don't want to know if there's fifty of them. Just give me an idea, will you, please?

MR. THOMPSON: Okay. There's a May 5, 2010, Meghan Johnson, Don Nelson -- to Don Nelson. And May -- another one on May 5, Meghan

Johnson to Don Nelson and another one on May 6. This is all -- looks like it's actually all one e-mail chain, May 6, 2010, Dr. -- from Nelson to Carter.

MR. MORIARTY: Is that it?

MR. THOMPSON: Yes.

Q. And your initial communication in this litigation, was it with Teresa Toriseva.

A. It was, yes.

Q. How do you know Teresa?

A. She asked me to consult in a case several years back.

Q. Okay. I didn't know Teresa was the chair of the PFC, but that's okay. Let me take care of two of the things in your stack that if we loaded by volume not weight they would take up the largest amount of space. One is Goodman & Gilman's Pharmacological Basis of Therapeutics, correct?

A. Yes, sir.

Q. It's got your name written on the book itself; is that right?

A. It does.

Q. Do you keep this in your home or office library?

A. I do.
Q. Pretty good text?
A. We recommend it to all second year medical students. Few read it, we do recommend it. It's a good book.
Q. And the other one is Baselt's Disposition of Toxic Drugs and Chemicals in Man, 8th Edition, correct?
A. It is.
Q. This also has your name written on the side of the book?
A. Yes, sir.
Q. I assume then you keep it in your home or office library?
A. I do.
Q. Do you refer your students to this book?
A. No.
Q. Why not?
A. They are not ready.
Q. You consider it as an excellent text but they may not be ready for it?
A. I consider it is a generally reliable reference text, yes.
Q. Okay. Thank you. Did you ever

look at the actual Digitek product label?

A. Could you expand on what you mean by label?

Q. Sure. When you talk about in FDA terms detailed patient labeling, that's what I'm talking about, some of the package inserts.

A. Sure. I just wanted to clarify that and without wasting your time, the short answer to that is no.

Q. Did you look at the Lanoxin detailed patient labeling?

A. I don't believe so.

Q. Those would be the FDA approved patient labeling that goes inside the tablet container, correct?

A. Yes, sir.

Q. Have you looked at any deposition testimony?

A. No.

Q. Other than representatives from either Ms. Toriseva's office or Mr. Thompson's office, have you discussed this litigation with anybody else?

A. No.

Q. Do you have any special training

in either regulatory quality assurance or quality control as it pertains to the pharmaceutical industry?

A. Yes.

Q. Tell me what training you have in that.

A. Well, I have a doctorate in clinical pharmacology from the University of California San Francisco and the curricula involved basic organic chemistry, pharmaceutical chemistry, qualitative analysis, quantitative analysis, study of FDA rules and regulations and quality control procedures and laboratory exercises in qualitative and quantitative pharmaceutical analysis and I spent a good deal of time in the pharmaceutical chemistry laboratory during the time period of '64 to '70 because at that point I was exploring the possibility of pharmaceutical chemistry as a future. So I do have background training and laboratory experience in pharmaceutical quality control from an experimental point of view, from a pharmaceutical chemical point of view and from a legal and regulatory point of view. The

licensing examinations in pharmacy require demonstration of a familiarity with FDA rules and regulations.

Q. Have you worked in quality control chemistry labs since the mid '70s?

A. Yes. I was involved in a clinical trial with a preparation for the removal of condyloma acuminata which are venereal warts, and we prepared and did manufacturing and quality control on the experimental product which was a preparation containing oxalic acid and some nitrates that were heated and had to be prepared in a very specific manner. And then we did quality control on the product prior to using these preparations in phase two human clinical trials, and this would be in the 1980s.

Q. Have you ever personally been involved in testing digoxin tablets for either assay content, uniformity, stability or dissolution?

A. I honestly don't know the answer to that question. I may have done that in a laboratory setting. I just don't remember specifically yes or no.

Q. Tell me in general what you now do day-to-day professionally as -- in your various capacities including emeritus professor?

A. Well, I have multiple responsibilities. My first responsibility is as associate director of the Drug & Poison Information Center, and we are the poison control center for southwest Ohio and we have about two hundred people in the organization. We handle all the overdoses, adverse reactions and poisonings for southwest Ohio. And I have been with that organization since 1972. And so it involves the day-to-day management of accidental drugs and poisonings, sometimes intentional drug poisonings. There's a certification examination for handling toxic overdoses and I spent two thousand hours at some point handling toxic overdoses and sat for an examination as a certified prevention information specialist and I've been handling responsibilities at the poison center since 1972 and continue to do that.

Q. Let me just interrupt for one second. The Cincinnati Poison Control Center --

A. Drug & Poison Information Center, DPIC.

Q. Is it part of this AAPCC annual report of the MPDS, do you know?

A. Yes, I do. The Drug & Poison Information Center is a part -- you're going to have to ask the question more specifically. I don't know what you mean. Yeah, we contribute data to this. Organizationally they don't run us.

Q. Okay.

A. I don't know what your question is.

Q. Well, there's another plaintiffs' expert in this case named Dr. Marc Semigran. Have you seen his report?

A. Dr. Marc --

Q. Semigran.

A. No, don't know him. Haven't seen his report.

Q. Among the things he listed in an appendix was the 2006 annual report of the American Association of Poison Control Centers National Poison Data System.

A. Okay.

Q. And if you go to the list of the poison centers that are participants the Cincinnati Drug & Poison Information Center is listed.

A. Okay.

Q. So does your -- the center of which you're the associate director contribute to this database?

A. We send some data to them, yes.

Q. I interrupted you. I wanted to know what else you do in your weekly duties.

A. Well, my duties vary over the period of a year, okay? From -- certainly twenty-four/seven, we provide drug and poison information center services to southwest Ohio.

Q. Actually I want to know what you do, not what they do. What your job is.

A. I do supervise that function. That is my job. My job is to handle difficult problems. On Tuesdays we sit and go over all the overdose cases that have happened in the past week with the people who handled the cases to review their performance and to be sure that what they are doing is accurate and appropriate.

Q. Do you get a paycheck from the Cincinnati Poison & Drug Center?

A. I get a paycheck from Cincinnati Children's Hospital because the DPIC is administratively under the department of resource development and public relations of the Children's Hospital.

Q. And then you get a separate paycheck from the University of Cincinnati for your faculty position on that side?

A. I do.

Q. Tell me what your faculty role is currently at the University of Cincinnati?

A. Well, my faculty role is supervising medical students, clinical fellows, nursing students, pharmacy students at the poison center.

And in terms of the college of medicine, the medical students are a part of the college of medicine as are medical residents as are emergency room residents as are pediatric residents, all of whom come to the drug and poison center for externships and teaching and supervision that I perform.

Q. Do you do any didactic classroom

teaching?

A. Yes.

Q. What courses do you teach?

A. I'm responsible for a course in basic pharmacology which is given on the main campus at the University of Cincinnati. It's a thirty-hour survey course. I also do continuing education. I do probably sixty hours a year various kinds of continuing education, lectures. I have been in the past the co-director of the medical school pharmacology course. I handle small groups, sessions in the second year medical school pharmacology course. I give lectures in the second year medical school pharmacology course in the areas of analgesiology, toxicology, adverse drug reactions, drug interactions and clinical pharmacology.

Q. Have you actually ever been an employee of a pharmaceutical company? Not a consultant, an employee.

A. I have been employed at various times by companies involved in the area of the performance of clinical trials and in that capacity have contracted with pharmaceutical

companies for the clinical trials that we have performed.

Q. At the time you did that you were still presumably on faculty at University of Cincinnati?

A. Yes, I was.

Q. Okay. So you didn't go to a pharmaceutical company every day to work?

A. I went to a separate facility in a separate building and performed clinical trials for a contract from multiple pharmaceutical companies.

Q. Have you ever been an employee of the FDA?

A. No.

Q. Do any of the classes that you teach involve the analytical chemistry of either immuno assays of blood or assays of solid oral dose form pharmaceuticals?

A. I teach about the use of the results of such tests. I do not currently have any classes where I teach quantitative, analytical, pharmaceutical chemistry. Obviously drug assays involving immuno assays, I teach about how to interpret those and we use

those every day in toxicology.

Q. Do you own or refer to the book Fundamentals of Analytical Toxicology by Flanagan, Taylor, Watson and Whelpton?

A. I don't own it. What was the other part of the question?

Q. Refer to it from time-to-time.

A. I have no idea whether I refer to it or not.

Q. Do you receive and regularly review journals in your field?

A. I do.

Q. Tell me a few of the more prominent journals that you review on a regular basis.

A. New England Journal of Medicine, ASCPT Journal, AACP Journal and Science. Oh, and I get Clinical Toxicology. That's the publication of AAPCC.

Q. I assume that over time you have had some education and experience in topics related to cardiology?

A. Yes.

Q. Epidemiology?

A. Yes.

Q. Nephrology?
A. Yes.
Q. How would you explain to me the difference between what you do and what a medical doctor does so far as the analysis of drug overdoses might be concerned?
A. I don't know what the question means.
Q. Sure. Well, since you're not a licensed physician in any state, you can't work in an emergency room and actually diagnose and treat patients who might have a drug overdose, correct?
A. Yes and no.
Q. Okay. That's what I'm trying to find out. What's the difference between the doctor, the medical doctor who does that and your role regarding that specific subject?
A. It's not as clear as you might think in the real world. There are -- there's overlap between what clinical pharmacists do in emergency room settings across the country and -- some of them work in emergency rooms and are very active in the process of diagnosis and differential diagnosis of the drug and chemical

intoxications, particularly people with advanced education in toxicology and clinical pharmacology.

Q. Do you have consulting privileges at any hospitals?

A. I consult on patients at Children's Hospital and University of Cincinnati Hospital to look at patients.

Q. Do you have to apply to the hospital for consulting privileges?

A. Typically the consultation is requested with respect to a very specific issue relating to toxicology and the information is given to the physician, documents are provided, sometimes an entry is made in the chart.

Q. If I go to the University of Cincinnati Hospital and subpoena their records and ask whether you have privileges officially at that hospital, is it yes or no?

A. I'm not a physician. I don't have admitting privileges at that hospital, no.

Q. I understand that. Do you have consulting privileges officially at the hospital?

A. I'm not aware that there is such a

thing as official consulting privileges. What I know is that since 1972 physicians from that hospital and other hospitals routinely ask for and receive a consultation and advice from me and other specialists in toxicology at the poison center.

Q. Do you officially take call at any hospitals?

A. No.

Q. Have you ever studied any of the University of Cincinnati Medical Center statistics to see if there was a spike in complaints about digoxin any time between 2005 and the first half of 2008?

A. No.

Q. In looking at Exhibit 41, your CV, I did not see that any of the articles that you published were directly about digoxin. Were there any?

A. Yes.

Q. Tell me which ones are directly about digoxin.

A. Okay. Page nine, number three.

Q. Let's stop there for a second. Does that just have a section about digoxin --

is there just a section about digoxin in there among many other drugs?

A. There is.

Q. Are you the editor of this book or the author?

A. We reviewed it. The poison center reviewed it.

Q. Do you know who wrote the section about digoxin for that book?

A. Well, each year we go through and revise what needs to be revised, so I guess I did.

Q. Was the --

A. If anything needed changing, we changed it.

Q. Do you know who the original author on the section on digoxin was?

A. No.

Q. Is the fifth edition the last edition of that book?

A. No.

Q. When was the last edition of that book?

A. Probably last year.

Q. What other books or what other

publications are directly about digoxin?
A. Page twelve, number three.
Q. Okay. What else?
A. I'm looking.
(Pause in proceedings.)
THE WITNESS: I think that's it.
(Thereupon, Defendants' Exhibit 40, a report authored by E. Don Nelson, Pharm.D., was identified for purposes of identification.)
Q. Handing you what's been marked as Exhibit 40, that's a copy of your report?
A. Yes, sir.
Q. And at page two in the third paragraph -- I'm sorry, part two, not page two. Part Roman numeral II?
A. That's on the first page. Okay.
Q. In the third paragraph, you say I have consulted on numerous cases of digoxin toxicity since 1972.
A. Um-hum.
Q. Do you see that?
A. I do.
Q. Do you know how many cases?
A. I don't know a number. It's lots and lots.

Q. When was the last time?
A. I don't recall.
Q. Are you talking about consulting --
A. Wait a minute, I do too recall. It was about a week ago.
Q. Are you talking about consulting in the setting of the poison center or in your work as a faculty member at the University of Cincinnati or are you talking about litigation consulting?
A. Well, all three are true. I handle -- I've handled thousands of cases at the poison center, and of those thousands of cases over the last thirty-eight years, a number of them have involved digitalis. I have dealt with digitalis in forensic cases over the years and I have dealt with cases clinically that made it to the hospital and I have been teaching on overdose cases.
Q. What kind --
A. So all of those are true.
Q. When you say forensic cases, are you using that as a different term for litigation?

A. Forensic cases to me means anything that involves the law. They may be criminal, they may be civil.

Q. So do you have any idea how many forensic cases in which you have been involved have involved digoxin?

A. I don't have a number. Coincidentally many of the patients in med mal cases are taking digitalis. You asked the question previously whether I could recall or whether these federal cases specifically involved digoxin as the primary issue and I said I don't think so. I don't know whether any of the cases in the last thirty years have involved digitalis as the primary agent.

Q. Have you ever been involved in a pharmaceutical products liability case in which digoxin was the primary agent involved?

A. No.

Q. In the consulting work that you have done regarding digoxin, in other words, forensic or not, have some of those cases had to do with intentional overdose?

A. I don't know the answer to that question. It's possible.

Q. Have any of those cases involved accidental overdose?

A. I don't know the answer to that question. It's possible.

Q. Have you ever rendered an opinion before today in a forensic case that a digoxin product was outside its specifications or defective?

A. I don't think so.

Q. Have you ever done any pharmacokinetic studies regarding digoxin?

A. Could you refine that question?

Q. Sure. Either in animals or humans, dosed them with digoxin and measured serum levels over time to establish pharmacokinetic parameters for the drug?

A. I may have done that clinically. I haven't done it in an organized clinical trial if that's what you're asking.

Q. When you say you may have done that clinically, what do you mean?

A. I mean, I may have done it clinically, dosed a patient and measured levels. I don't remember.

Q. In what kind of setting?

A. A hospital.
Q. Under the supervision of a physician?
A. Yes.
Q. Now, do you remember specifically doing that or is this something you possibly have done?
A. It's something I possibly have done.
Q. Have you ever published any epidemiologic studies about outbreaks of drug reactions or toxicity?
A. Yes.
Q. Can you identify those in your CV?
A. Sure.
Q. And do you know what the drugs involved were?
A. Lots and lots of drugs.
Q. Well, are you about to refer to lots and lots of papers?
A. Yes.
Q. Then let's move on to something else. Did any of the --
MR. THOMPSON: Let me interrupt and say Dr. Nelson had a hip replaced about six weeks

ago and he occasionally may need to move around.

THE WITNESS: That's okay.

MR. THOMPSON: I want to encourage him to speak up if he wants a break or needs to walk around.

THE WITNESS: I had a knee replaced. But that's fine.

Q. As long as you can walk around and talk at the same time. Have you ever published any epidemiologic studies about outbreaks of digoxin toxicity?

A. No.

Q. Now, in an article that you wrote back at the end of the '70s, you reported that there were probably fifty to sixty thousand prescription drug products that have the potential to cause harm to patients. Do you know whether those numbers have gone up or down?

A. Well, let me see the publications and we can discuss it.

Q. I just want to know if you think the numbers have gone up and down. I really don't want to discuss it.

(Pause in proceedings.)

THE WITNESS: I think that the number of drug products has increased since the 1970s.

Q. No, my question is are there more than fifty to sixty thousand prescription drug products that have the potential to cause harm to patients?

A. I would think so, yes.

Q. And then I believe there's a separate article called Evaluation of a New Approach to Geriatric Drug Education -- I'm sorry, let me rephrase that. Same article I just showed you from 1978, you reported a hundred thousand to five hundred thousand nonprescription drug products available over the counter that had the potential to cause harm. Has that number changed?

A. Number of over-the-counter drug products?

Q. Yes.

A. I don't know the answer to that question. Some of them have been recalled and there's certainly been some new ones. I don't know if the total number has gone up. I don't remember the answer to that question.

Q. Now, in 1982 you wrote this -- or

co-authored this paper called the Evaluation of a New Approach to Geriatric Drug Education, and in it you reported that twenty-three percent of the elderly nursing home patients are prescribed drugs which are known to interact. Okay? Do you know whether those numbers are probably the same today as they were back in 1982?

A. The number of medications being prescribed for the elderly in general has increased since 1982, the average number of prescriptions per elderly person.

Q. So would you agree that a substantial number of elderly patients -- elderly nursing home patients are prescribed drugs which are known to interact?

A. Yes.

Q. And I believe in this paper you also reported that seventeen percent of elderly nursing home patients and twenty-five percent of other elderly patients would be hospitalized at least once because of an adverse drug reaction. Do you know whether those numbers are substantially different in 2006 than they were when you wrote this paper in 1982?

A. No.
Q. No, you don't know?
A. I don't know.
Q. And I would assume that even back in 1982, not all these hospitalizations for adverse drug events were because of defective medicine; is that true?
A. That the hospitalizations were not sequitur to defective medicine?
Q. I didn't use the word sequitur, but not due to.
A. I think that the assumption is that the medications involved in those incidents were within manufacturer's specifications.
Q. Broadly speaking, there are a number of reasons that elderly patients have adverse drug effects, correct?
A. There are, yes.
Q. Now, at page one sixty-six of your 1982 article, there was a questionnaire that was duplicated within the text of the article.
A. Why don't you let me see that.
Q. Sure. Let me read it first. And question number five says generally the more

medicines a person takes, the greater the risk of developing an adverse reaction. And this is supposed to be a yes or a no question.

A. Okay, I understand now. I don't need to see it.

Q. Is the answer yes? Generally the more medicines a person takes the greater the risk of developing an adverse reaction?

A. Yes, that's generally true. Not absolutely, but generally.

Q. And taking a number of different medicines at a time is generally called polypharmacy, is it not?

A. Yes.

Q. Do you know how many digoxin prescriptions are written in the United States on an annual basis?

A. I don't know the exact number. It's millions.

Q. Do you know anything at all about the relative market share of any of the manufacturers of digoxin that are sold in the United States?

A. I don't have statistical data. My assumption is that Lanoxin has a significant

part of the market and obviously Digitek has a significant part of the market. I don't know the rest.

Q. Now, I've asked you how many prescriptions are written and you said millions, but do you know how many people in the United States are on digoxin in a year?

A. Well, millions.

Q. Among the materials that were sent to you of various deposition exhibits from company witness depositions in this litigation, some of them are warning letters, form 483s, things of that nature?

A. Yes, they are.

Q. And did you look at those?

A. I did.

Q. In the course of your weekly duties, how often do you look at an FDA form 483?

A. Not regularly.

Q. Would the same be true of FDA warning letters?

A. No, we get those fairly regularly at the poison center and through electronic media because they involve medications that we

have to deal with on a daily basis so we stay fairly up to date on warning letters.

Q. I'm not talking about warning letters from pharmaceutical manufacturers. I'm talking about FDA warning letters.

A. Well, I'm not a manufacturer so I don't receive manufacturers' warning letters.

Q. Well, that's my question. I assume in the course of your regular duties you get all kinds of correspondence like dear doctor letters, changing of label information from FDA or manufacturers; is that true?

A. Yeah. It's not that cut and dried, Counselor. On a daily basis I get information on results of FDA warnings to manufacturers which have resulted in recalls or warnings to health professionals.

Q. Well, before you were consulted in this litigation, did you receive any correspondence between FDA and Actavis such as form 483 or warning letters?

A. No.

Q. Do you know whether the University of Cincinnati -- well, I'm sorry, does the University of Cincinnati have a pharmacy

school?

A. It does.

Q. Do they have an analytical laboratory?

A. Yes. There are some laboratories that are analytical in the college of pharmacy, yes.

Q. Do you know whether the University of Cincinnati analytical labs ever test solid oral dose pharmaceutical products?

A. I don't know. I assume they do.

Q. Do you know anything about the methods that they use to do it?

A. Yes.

Q. Well, do they use the USP method of high performance liquid chromatography to do that?

A. I would assume they use the USP method, whatever it is. There are a number of standard procedures that are used in pharmaceutical chemistry, qualitative analysis laboratories, and they involve several different techniques.

Q. Do you consider yourself to be an expert in the difference between the accuracy

of the techniques of single beam UV methods versus HPLC methods?

A. I've done both. I have some familiarity with those analytical procedures, how they are done, physical chemical principles on which they are based and their relative usefulness.

Q. Do you know anything about the actual quantitative difference between those two methods and API content assessment in solid oral dose forms?

A. I know that they are different techniques and in general the HPLC method is -- for digoxin analysis is generally regarded as more accurate than the UV method which is more of a -- is a less precise method for measuring digoxin content of tablets.

MR. THOMPSON: Doctor, Mr. Moriarty is not going to be through within the next hour so I would suggest if you want to that you take periodic breaks at logical stopping points.

THE WITNESS: Sounds like a good idea.

MR. MORIARTY: Let me ask a couple more and maybe that will be a logical stopping

point. My goal is to be done today -- early today.

Q. Do you whether or not the University of Cincinnati pharmacy school has in place a standardized digoxin testing procedure for tablets?

A. I don't know if they have one in place today. I know that over the last thirty-eight years they have.

MR. MORIARTY: Okay, you want to take a break, we can take one now.

THE WITNESS: Thank you.

(Recess held.)

Q. Tell me about your direct personal experience with pharmaceutical recalls.

A. Pharmaceutical recalls, okay. I functioned as a pharmacist early on in my career and we would receive correspondence from pharmaceutical manufacturers indicating that for some reason the product that had been shipped and many times dispensed was defective, misbranded or adulterated for some reason and we proceeded to identify the inventories we had in the various pharmacies and then try to proceed as best we could to make a judgment

about whether -- what could be done regarding the patients who had received the recall. So my experience was early on in my career and functioning as a pharmacist.

Q. And when was that?

A. When was that? 1970 to '72, '73, something like that.

Q. Have you had any personal involvement in the pharmaceutical recalls since that time?

A. Well, we deal with them all the time at the Drug & Poison Information Center. We get information and we get calls from people who have taken various medications which have been recalled for various reasons. Over the years there have been a number of medications that have been recalled for various reasons, contamination or the emergence of adverse drug reactions from medications which were not outside the label.

Q. And when you say various reasons, you would agree with me product can be recalled even if they do turn out to be within their labeled specifications, true?

A. Certainly. Medications can

develop an adverse reaction that was not anticipated by any of the previous work and be recalled, yes, Vioxx being an example of that kind of medication. Baxter had an episode with contaminated heparin. These things happen.

Q. Okay.

A. Unfortunately, sometimes people die.

Q. Has anybody ever shown you -- I'm sorry, let me rephrase that question. Have you ever weighed or measured any Digitek tablets?

A. No.

Q. Have you personally commissioned the testing of any Digitek tablets for whether they were within the labeled specifications?

A. No.

Q. Now, you have used the word adulteration a couple times, and at the first page of Exhibit 40 in the last paragraph you even mentioned that you're familiar with the FDA rules and regs regarding misbranding and adulteration. Do you see that? Last paragraph on the first page.

A. Yes, um-hum.

Q. To your knowledge has FDA ever

said that adulteration means that all the tablets in the case of a solid oral dose were outside the specification?

MR. THOMPSON: Object to the form.

THE WITNESS: What it means is that nobody knows the answer to that question.

Q. Are you done with your answer?

A. Yes.

Q. Okay. And adulteration as far as you understand it, is defined by part of the Food & Drug & Cosmetic Act; is that right?

A. It is.

Q. Just for an extreme example, there could be a problem with the way the label itself is affixed to a container and that could fit the definition of adulteration; is that true?

A. I don't know the answer to that question.

Q. All right.

A. I think that would be mislabeled, but I'm not sure.

Q. But it doesn't necessarily mean that the tablets in that container are outside their specifications, right?

A. Can't prove they are, can't prove they aren't. That's what it means.
Q. That's what adulteration means?
A. Yes.
Q. Well, what do you mean can't prove they are or can't prove they aren't?
A. Well, you got a million tablets and your quality control procedures can't assure you of the content of the tablets. That's the situation in front of us.
Q. Well, they can be tested, can't they?
A. Each tablet can be tested, yes. Could be. Maybe.
Q. But your understanding of adulteration, there can be reasons that lead to calling something adulterated that has nothing to do with whether they are within the labeled specifications for active pharmaceutical ingredients; is that true?
A. I don't know. What we have here is a lapse in quality control that cannot assure us of the content.
Q. That's not what I'm asking you. I'm asking about your understanding of the term

adulteration. Okay?

A. My understanding of the term adulteration with respect to this case is that the quality control was not there to give that assurance.

Q. That's not what I'm asking you. I'm asking you about your general understanding of the term adulteration.

A. My general understanding is that the manufacturer of the product in question cannot assure the content of the product.

Q. All right. So you will not answer my questions generally. You just want to refer back to this case?

A. I have. You asked what adulteration is. Adulteration is the problem where the manufacturer cannot guarantee the contents of the product and that's -- that happens to be the situation in this case as determined by the FDA, not Dr. Nelson.

Q. So what you're saying is -- no I'll withdraw. Have you ever read the July 2009 statement made by the FDA on its website about the Digitek recall?

A. I don't know the answer to that

question. I don't think so but I'm not sure.

Q. Would it be of any interest to you to know what the FDA said a year and a quarter after the Digitek recall about that situation?

A. I don't know. Depends on what it says. Can't answer a question about something I haven't read.

Q. Well, did it interest you to what FDA said about it in these warning letters and 483s that you looked at in your review of this case?

A. Somewhat, yes.

Q. Do all prescription medications have risks?

A. They do.

Q. Even in labeled appropriate doses?

A. They do.

Q. Those risks can be serious up to and including death in some cases?

A. They can.

Q. Does that include digoxin?

A. It does.

Q. The analysis of cause and effect or causation, do you consider that to be a scientific process?

A. Not in the strict sense, no.
Q. Why not in the strict sense?
A. Because you don't have controls. What you have is hundreds of thousands of individual -- millions of individual patients taking prescription medications, including digitalis in various ways, essentially no two of which are the same, and so it's not what one would design if somebody was designing a scientific experiment. What we have is what I consider an uncontrolled experiment which is the practice of medicine, the practice of clinical pharmacology. Each patient is an experiment.
Q. Each patient is an individual analysis?
A. It is.
Q. And the patients come in various weights and ages, correct?
A. They do.
Q. A variety of conditions with their heart and their kidneys?
A. They do.
Q. And they can have widely varying responses to various doses of digoxin, correct?

A. Well, there's some predictability. Otherwise there wouldn't be a science of pharmacology.

Q. Sure.

A. There's some variation, but the digitalis always goes to the same receptor and does the same thing.

Q. Sure, but they may have widely different clinical responses?

A. Well, when they respond they do the same thing, heart beats stronger and they have better circulation, so it's not true that some of them have responses all over the board.

Q. Well --

A. They have predictable responses. If they respond to the drug, they respond in a classic characteristic way of increasing the strength of their heartbeat. That's the whole point of giving the drug and if you give the right dose, it happens.

Q. Is assessing causation a scientific inquiry at all?

A. Well, there -- there's some principles of timing and intensity and expectation of effects versus adverse

reactions. If you give a drug and something peculiar happens at the same time, you have a high index of suspicion that giving the medication might have had something to do with it. It is a complex judgment-heavy area of undertaking and it requires some experience and knowledge of the patient's pathophysiologic condition and the effects of the medication -- of medications that the patient is taking.

Q. And you certainly want to rule out other potential factors of the adverse event, correct?

A. If possible, yes.

Q. I asked you before whether you had studied the University of Cincinnati's statistics and whether they had had a spike of digoxin. Did you do any study like that at the poison center?

A. No.

Q. Do you know how many calls the poison center received after the April 25th recall regarding Digitek?

A. I do not.

Q. Do you know how many calls the poison center received prior to April 25th,

2008, regarding Digitek?

A. I do not.

Q. Are you licensed to prescribe in the state of Ohio?

A. No, not under usual conditions. There are some facilities that have clinics for hypertension, diabetes, cardiovascular disease and so forth that have people with my training and background managing drug therapy. I personally don't happen to do it, but people with my training do.

Q. Are there a number of different reasons why someone can have an elevated serum digoxin level?

A. Yes.

Q. Are there a number of different reasons why someone can have clinical signs and symptoms of digoxin toxicity?

A. Yes.

MR. MORIARTY: I didn't have these marked. Can we mark -- I don't know how high my office has gone in this numbering. I wasn't told that so I'll mark a couple of articles. How do you want me to mark them? Want to mark them Dr. Nelson Exhibit 1 or 2 or do you want me to just

pick a number out of thin air realizing there may be a gap?

MR. THOMPSON: I'll tell you what would make me happy. The last one you used was Defendants' Exhibit 40.

MR. MORIARTY: 41.

MR. THOMPSON: No, the last one you questioned him about was 40, right.

MR. MORIARTY: Correct.

MR. THOMPSON: To me, I would actually like it if you put them as Defendants' 40-A, B, C, D, like that. That way they are closer together in the chronology. I assume that you premarked like Semigran and other people. That's what we're listening to.

MR. MORIARTY: Right.

MR. THOMPSON: To me I would like it temporally close to this. Is that something --

MR. MORIARTY: Sure.

(Thereupon, Defendants' Exhibit 40-A, an article entitled digitalis Toxicity authored by J. Thomas Bigger, Jr., M.D., was marked for purposes of identification.)

MR. THOMPSON: Doctor, you have been handed a document that you've not reviewed before

this deposition so you are entitled to take the time you need to familiarize yourself. While it may be Mr. Moriarty is only going to want to ask a question or two, but you have the opportunity to review it until you're satisfied that you recall it or understand it.

THE WITNESS: Very good.

Q. Have you ever seen this article by Dr. Bigger before?

A. I don't know the answer to that question.

Q. It's from the Journal of Clinical Pharmacology in 1985. Is this a journal that you would have been reviewing back then?

A. Probably not.

Q. The only thing I want to ask you about is on the second page of this article which is page five hundred and fifteen. Do you see table one there?

A. I do.

Q. Would you agree with me that that is a good concise summary of the causes of digoxin toxicity?

A. Some of them.

Q. Are there any that you disagree

with?

A. Well, there are -- some apparently glaring omissions, but other than that, the things that are listed here are -- are sometimes associated with digitalis toxicity.

Q. What are the glaring omissions?

A. Oh, here's drug interactions, he's got it under reduced volume of distribution which is not true, but, okay. There are a number of other sources of digitalis toxicity out in the real world. There are a number of plant sources of cardiac glycosides which are problematic that we see at the poison center. He's got drug interactions under reduced volume of distribution and that's -- certainly it's not true that all drug interactions are attributable to reduced volume of distribution. To bioavailable, an individual patient's bioavailability is fairly constant over time so it's a table in a paper, got some -- yeah, there's some yes things here, and no, there's some no things here.

Q. Well, perhaps he was referring to the tablets being too bioavailable.

A. I have no idea what he's referring

to.

Q. So can patients develop elevated serum digoxin levels or clinical signs and symptoms of digoxin toxicity when taking doses that are within the tablet specifications?

A. They can.

Q. Why is that, in general?

A. There isn't any general. They are all specifics. The specifics are that the -- there is a science called pharmacokinetics which is the other part of pharmacology which is pharmacodynamics is what the drug does to the body, pharmacokinetics is what the body does to the drug. And the pharmacokinetics of digoxin are compound, complex and are influenced by the pathophysiologic state of the patient and what the patient is doing, what the patient is eating, the patient's environment, medications the patient is taking, diseases the patient gets intermittently, concomitant medications including other things a patient takes in. So given a constant dose, there are a number of things that can cause the pharmacokinetics which means the half life of plasma level, the volume of distribution,

elimination rates constant for digoxin can change. When these things change, if the eliminations decreased over a long period of time you can have accumulation of the drug. So yes, it can happen and there are multiple reasons that it can happen, including there's too much drug in the body or too little drug in the body, that the heart doing its thing in the other places it needs to be to be therapeutic.

Q. So digoxin toxicity is a known potential risk of the drug?

MR. THOMPSON: Objection to the form.

THE WITNESS: Digoxin toxicity sometimes occurs. When it happens, obviously it's caused by the drug. Kind of a circular question.

Q. Do the elderly tend to take more drugs than younger people?

A. They tend to take numerically larger numbers of drugs than younger people because in general the elderly have more -- have accumulated more diseases over their lifetime.

Q. Is the population of elderly patients on polypharmacy at increased risk for adverse drug events?

A. They are, but again, that's a general answer and the specifics depend on what specific drugs the elderly are taking. Each medication has its own spectrum of possible adverse reactions and interactions with the other medications that they are taking.

Q. Well, the elderly, because they are at increased risk for heart problems, do tend to take more cardiovascular drugs, do they not?

A. They do.

Q. Have you studied anything about the incidence of accidental overdose or noncompliance with drug prescriptions in the elderly?

A. Yes.

Q. What is your understanding of whether the elderly have higher rates of accidental overdose or noncompliance than their younger counterparts?

A. Well, we call it adherence these days. It's the new speak. And in general, with a larger number of tablets per day and a number of different dosing regimens and times and in some patients with attendant mental

deterioration, their adherence rates tend to be lower than people who are taking fewer medications and who have their complete mental faculties about them.

Q. In other words, there is literature out there which talks about the elderly, especially in polypharmacy and higher rates of nonadherence, correct?

A. Generally, yes.

Q. And higher rate of adverse drug events?

A. They do.

MR. MORIARTY: Could you mark this as 40-B.

(Thereupon, Defendants' Exhibit 40-B, a one-page sheet, page 581, from Drugs in the Treatment of Heart Failure, was marked for purposes of identification.)

Q. I'm handing you Exhibit 40-B which I'll represent to you is a table in a chapter --

A. I don't have it.

Q. I'm sorry. It's a table from a chapter in Braunwald's cardiology text. First of all, do you have Braunwald's cardiology text

in your home or office reference library?

A. No.

Q. Have you ever seen this table before?

A. I don't know.

Q. From your knowledge of digoxin and drugs with which it may interact, do you know whether this is a reasonable and reliable table about that subject?

A. It's a table in a textbook about interactions with digoxin. I'm not going to validate it as being gospel.

Q. I didn't ask you whether it was gospel. I asked you whether to you in your experience it seems reasonable?

A. Don't know the answer to that question. This is not the way I deal with drug interactions. The way I deal with drug interactions is to go to the original publications. For example, St. John's wort down here at the bottom is not a predictably dosed medication. It's a dietary supplement and to opine that it always increases digoxin levels is probably not valid. Drug interactions are sometimes things rather than

always things and part of the education of medical practitioners is that when you have a patient taking digoxin along with other medications, it's important to go to the original literature regarding the interaction or alleged interaction because many times these are a result of a case report or two of such interactions or that the drug is a member of a family of drugs that always seem to interact with digoxin, but there's really no specific case report. Using this kind of a table is maybe sometimes useful. There are difficulties in going from concluding that carvedilol always increases the blood level of digoxin. So what is the table, it's a table of reported drug interactions which sometimes occur, sometimes don't, and when they occur they may or may not be clinically significant. That's what this is.

Q. Okay. So when you say go back to the source, is this Goodman & Gilman's book one of the sources to which you would refer about drug interactions?

A. Not usually, no.

Q. Would you go to the detailed

patient labels reproduced in the PDR?
A. No.
Q. What source would you use?
A. I go to DRUGDEX.
Q. DRUGDEX?
A. DRUGDEX.
Q. Is it an on-line compendium or textbook?
A. It's a toxicologic and pharmacologic database which is use by the drug and poison information centers in the United States and it's A, generally reliable and B, tends to quote the source documents for interactions.
Q. Are you familiar with Lexi-Comp ONLINE interaction lookup?
A. I've heard of it.
Q. Do you know anything about how reliable it is as a source for drug interactions?
A. Yes.
Q. And is it reliable?
A. Sometimes. Sometimes yes, sometimes no. Garbage in, garbage out.
Q. Are you saying it's all garbage or

some of it is?

A. I'm saying that drug interactions are an extremely complex area of endeavor and that one needs to go to the source document that constitute the reports and look at them and see what the reality is about the report and make some judgment about whether that report has any relevance to a clinical situation that you're dealing with. You can't just put a rubber stamp on some database and say this is always reliable. That's a big mistake.

Q. Is Drugs.com generally reliable?

A. I don't use Drugs.com for any kind of complex questions.

Q. Well, does that mean it's not generally reliable or it's just not your preferred source?

A. Both. I wouldn't say it's not generally reliable or generally unreliable. It's a popular online database put together with not the kind of quality control procedures that a competent licensed professional with thirty-five years of experience wants to use in the process of treating a patient. You want to

go back to the source documents because you want to minimize the possibility that you make an error.

Q. When you say the source documents, are you talking about published medical literature?

A. Yes. For each of those drug interactions, there's a stack of papers that has to do with the basis for the table in Braunwald, the Lexi-Comp, the Drug.com, and reality is incredibly more complex than anything you can put in a chart. You have to go back to the source documents to make a clinical judgment. You can't just pick the stuff out of a chart and say this is the way to practice medicine. You're going to make mistakes if you do that.

Q. I had asked you a little bit earlier about this increased incidence of adverse drug events among the elderly?

A. Yes.

Q. We had already talked about that. And that occurs even when the elderly are taking medications at normal prescribed doses; is that correct?

A. Well, I don't know what a normal prescribed dose is, but they are taking -- it can happen if they are taking the drugs as prescribed, yes.

Q. And it can happen when the drugs prescribed are within their label specifications, correct?

A. It can, yes.

Q. If a patient has underlying renal insufficiency, does that increase the risk of adverse reactions to drugs cleared primarily by the kidneys?

A. Usually, yes, unless, again, dialyzed or something else.

Q. Does renal insufficiency increase the risk of digoxin toxicity?

A. It can.

Q. Are doctors supposed to customize doses based on their patients' renal status?

A. They are.

Q. What's glomerular filtration rate?

A. It's how much plasma is filtered through the kidneys per minute.

Q. Does it slow down with advancing age?

A. Generally it does, yes.
Q. Does renal function in general diminish with advancing age?
A. In general, yes.
Q. Why, briefly?
A. It decreases because there is deterioration of cardiac output, renal blood flow and the vascular feed to the kidney. Essentially, elderly pump less blood per minute to the kidney than younger people do per pound of body weight.
Q. Does muscle mass typically decrease with advancing age?
A. It does.
Q. And do you agree that serum creatinine underestimates the decrease in GFR with age?
A. To go from creatinine to GFR you need to use a different formula in the elderly so at a given serum creatinine level, somebody who's ninety years old generally has a lower GFR than somebody who's thirty years old with that same creatinine level.
Q. So, in other words, a serum creatinine in the upper or normal range may

already reflect impaired renal function in an elderly patient?

A. Right. Because what's happening is they are not making as much creatinine.

Q. Is digoxin toxicity fairly common?

A. Is it common? I don't know how to answer that question. It happens and we all -- all of medicine needs to know about it. We study it and we certainly see it occurring, so, yes, I would say it's relatively common, the toxicity that is -- for example, if you look at the toxicology section of medical school pharmacology courses, they all teach about digoxin toxicity and it's part of medical board, part of clinical practice. It's part of poison control so it's on the radar in terms of yeah, it can happen.

Q. Have you compiled any statistics just for digoxin toxicity from the Cincinnati Drug & Poison Information Center?

A. No, I have not.

Q. Have you compiled any separate statistics just for cardiac drug toxicity from the Cincinnati Drug & Poison Information Center?

A. I think we probably have that in the last annual report and certainly we've done that in the past to look at cardiovascular agents and which drugs are involved in overdoses.

Q. Let's talk about serum digoxin concentrations. Do you ever look at the results of those kind of tests?

A. Yes.

Q. Would you agree that there is no one SDC level that defines toxicity?

A. I don't know what you mean by SDC.

Q. Serum digoxin concentration.

A. Oh, okay. Well, what we know is that each lab has their own range for serum digoxin concentration, SDC, and if it's zero we don't have a drug being administered. If it's up to about five nanograms per mil, we think that some drug is being administered. At about one nanogram per mil is beginning therapeutic range. As the serum concentration increases progressively, we see an increased incidence of toxicity and adverse drug reactions in general, and in overdoses we tend to see very high levels of digoxin in the serum. We use it for

monitoring toxicity and making decisions whether we're going to give the antidote for digoxin which is Digibind which is an antibody that combines with the digoxin that has become available for treatment of digoxin overdose.

Q. Are you done with your answer?

A. I think so, yes.

Q. That wasn't really my question. My question is would you agree that there's no one serum digoxin concentration level that defines toxicity?

A. No, I don't agree with that. In general anything above one and a half to two is associated with toxicity and there's good data to support that.

Q. I want to read you a quote.

A. Toxicity is not independent of serum level, if that's what you're getting at. It varies in association.

Q. I want to read you a quote from the American College of Cardiology article by Tom Smith back in the 1980s. It says in terms of the management of individual patients, I would emphasize that no specific serum concentration exists that can be used to define

a clear boundary between the presence and absence of toxicity. Do you agree or disagree with that?

MR. THOMPSON: Object to the form.

THE WITNESS: Well, I answered the question before. The reality is, and it's published, that once you get above about two you have an increased incidence of toxicity as you go higher in serum level so if the good doctor is telling us that if you have got a serum level of ten nanograms per mil, you can't figure anything out from that, I would disagree with him and the point he's making, I think, is that you can't take an isolated serum level and deduce toxicity, but you can certainly increase your probability from one percent to ninety percent by looking at an appropriately drawn serum level which is appropriately drawn about six hours after the ingestion. So this is an isolated statement from an article that is making a different point than -- he's not saying that there's no correlation between toxicity and serum level and if he is, he's wrong.

Q. I just asked if you agreed with the quote.

A. Well, I assume you read it the way it's stated.

MR. THOMPSON: Objection. Asked and answered.

MR. MORIARTY: He didn't answer it. With all due respect he gave me a very long answer. He didn't say yes I agree with it or no I don't.

THE WITNESS: I don't agree with that statement.

Q. In the midst of your answer, though, you said you can't take a serum concentration and deduce toxicity from it. Do you agree with that?

A. I think that's what his statement is trying to say, I guess. I don't know.

Q. Well, do you agree with it if that's what it's trying to say?

A. No. I think that anything above two, you have an increased rate of toxicity. And the reason I think that is it's published data. So whatever he says, he says, and the data says otherwise.

Q. So anything above two, you have an increased rate of toxicity?

A. You do.
Q. My question is can you say that everybody with a 2.5, for example, has digoxin toxicity?
A. They have an increased probability and if you go high enough you get the ninety-nine percent, so, yes.
Q. In order to define that increased probability of whether they had digoxin toxicity, you would have to put it in a bigger context of an individual patient, correct?
A. No. There's published data that shows that anything above two increases the rate of toxicity.
Q. Not my question. My question is --
A. Your question is there some patient out there who has a twelve who doesn't have any toxicity, and the answer is probably not.
Q. All right. Well, my question is 2.5, not twelve. So there are patients out there who could have a serum digoxin concentration of 2.5 and not have digoxin toxicity, correct?

A. Maybe.
Q. So in order to figure out whether it's maybe or probably, you would want a greater context like an EKG and clinical signs or symptoms, correct?
A. That would be a next step, yes. Maybe a repeat level. Maybe you would stop the medication. You might do a lot of things. But the notion that there's no correlation between blood level and toxicity is untenable.
Q. Did I ask you if that was a true statement?
A. I think that's where you were going, yes.
Q. Really? I would like you to answer my questions, not read my mind. Okay?
A. I've done that.
Q. Dr. Smith says in this same article, under no circumstances can serum digitalis levels replace sound clinical judgment. Do you agree with that?
A. I don't agree or disagree with that statement. It's so -- it's out there.
Q. Do you agree with his next statement, an individual laboratory value

should never be used as the sole basis for determining the presence of drug toxicity or efficacy?

A. No, I don't agree with that statement.

Q. Okay.

A. That statement is so broad it can't possibly be true.

Q. Dr. Kristin Williamson and colleagues wrote a patient -- or an article about digoxin toxicity in the Archives of Internal Medicine in 1998, and in that article she says therapeutic drug monitoring improves patient care and likely contributes to the suspected decrease in digoxin toxicity, however, elevated concentrations alone do not constitute toxicity. Do you agree with that?

MR. THOMPSON: Object to the form of the question.

THE WITNESS: I think, again, you have clinicians pontificating about the significance of serum levels, and I think I have made it clear that as the serum level rises, you have an increase in probability of toxicity and ignoring that is not a good idea.

Q. What specific medical literature would you rely on to assess at what levels this probability increases and what harm increases along this -- increases along with it?

A. I would be happy to provide you literature.

Q. Is there any in the stack that you brought today that addresses that subject?

A. I think so.

Q. Which literature addresses that subject?

A. Hand me Goodman & Gilman.

Q. (Indicating.)

A. Read the digoxin.

Q. You have given me back Goodman & Gilman's 10th edition?

A. I have.

Q. Open to --

A. Digoxin.

Q. Page one thousand nine forty-eight, one thousand nine hundred forty-nine.

A. Right.

Q. And there are some references listed here.

A. Um-hum.
Q. Correct? Is that what you're pointing me to? Is that what you want me to look at?
A. That's the reference. You asked for the reference.
Q. So Mooridian, M double O R A D I A N, digitalis, An Update of Clinical Pharmacokinetics, Therapeutic Monitoring Techniques and Treatment Recommendations, and Clinic -- I'm sorry, Clinical Pharmacokinetics, 1988, Volume 15, Pages 165 to 179, and Smith and Haber, digoxin Intoxication, The Relationship of Clinical Presentation to Serum digoxin Concentrations --
A. There you go.
Q. -- in the Journal of Clinical -- is it Investigations -- 1970, Volume 49, Pages 2377 to 2386. So those are the references --
A. They are.
Q. -- that I should look to?
A. And they say what I said.
Q. Can patients have signs or symptoms of digoxin intoxication at levels that would be considered by the lab within

therapeutic limits?

A. Sometimes.

Q. Do you know at the University of Cincinnati Hospital what the lab range of therapeutic is on their serum digoxin concentration lab studies?

A. I'm not certain. I think it's in the range of one to two nanograms per mil. They probably send it out to an outside lab.

Q. Do you know of any published medical literature that says that renal failure or renal insufficiency is a complication or a risk of digoxin therapy?

A. There may be something out there someplace but kidney is not traditionally thought of as a target organ for digitalis toxicity.

Q. Can electrolyte imbalances, especially in serum potassium play an important role in diagnosing digoxin toxicity?

A. Sometimes.

Q. Can it be a cause of digoxin toxicity in certain arrhythmias?

A. Sometimes.

Q. Can it be caused by digoxin

toxicity in certain arrhythmias?

A. Sometimes.

Q. Is the same true for calcium?

A. Yes.

Q. So it can be the cause of toxicity or certain arrhythmias?

A. Yes.

Q. And caused by toxicity and certain arrhythmias, true?

A. Yes.

Q. How many times have you made reports to the FDA of adverse drug reactions?

A. I don't know the answer to that question. Probably made a few because we did clinical trials and there were adverse effects and those went -- those trial results, phase two trials all went to the FDA eventually, so several times.

Q. Have you ever made report to the FDA of adverse drug reactions outside your work in clinical trials?

A. I'm not sure. I may have. I don't know.

Q. Do you know whether you have ever made an adverse drug reaction report to the FDA

about a digoxin product?

A. I'm not sure.

Q. Have you made one in the last four years regarding digoxin?

A. Not a Med Watch report, no.

Q. Any kind of report to FDA about a digoxin product in the last four years?

A. Not personally, no. No.

Q. Did you instruct anybody who works for you or works with you to make such a report?

A. No.

Q. Have you been asked to draw any dose response curves as part of your work in this litigation process?

A. No.

Q. Do you ever draw dose response curves in your work as a pharmacologist?

A. I do.

Q. Have you ever drawn any for digoxin?

A. I don't know. Probably.

Q. If you were ever going to draw a dose response curve for digoxin, where would you get the data to do that?

A. From a clinical study, from the literature.

Q. From the published medical literature?

A. Yes.

Q. If you were trying to study dose and response, would you need to know the dose in the tablet?

A. Well, if you were getting tablets you would need to know that, yes.

Q. Let me rephrase my question. I don't want to talk about IV's or --

A. Yeah, you need to know the dose of the drug you're administering regardless of the dosing form, correct.

Q. And you would also want to know the frequency of the dose, correct?

A. Certainly.

Q. Have you ever -- I'm sorry, let me rephrase that. Are you familiar with any mathematical formulas that have been proven reliable to back calculate dose or duration based on serum digoxin concentrations?

A. Well, pharmacokinetics has equations for determining the plasma level at a

previous point in time given certain assumptions and information. If somebody took a big dose of Dig three days ago and you have a plasma level, a serum level today, you can figure out a range of what it was two days ago, yes.

Q. Do you know anything about the reliability of those formulas?

A. Yes.

Q. Can you tell me in what medical literature there is a reliable formula for that?

A. There are a number of textbooks of pharmacokinetics. They pretty much have the same kind of equations in them. It depends on what it is you're asked to do and the particulars of a situation. If somebody took thirty tablets of Dig ten minutes ago and you draw a level, it's not going to mean anything. If you wait two, three days, it could probably -- or twelve hours, you could probably figure out, you know, what the level was, say a few hours before that point. And the next day you can figure out what the level is and you can draw a curve of the level and get the half

life, but you have got an absorption component so it's complex. You can't answer the question in general. Is there a scientific formula for going backwards in time, the answer is sometimes.

Q. Do you ever use those formulas?

A. Yes.

Q. And what textbooks do you use to find the formulas?

A. Well, Goodman & Gilman's has got pharmacokinetic equations in it and they are published. They are public domain stuff.

Q. And I think you said earlier that the appropriate time to draw a serum digoxin concentration is six hours after the last dose; is that correct?

A. Generally a minimum of six hours because you have got absorption and then you have got distribution and so forth. And that's the same kind of things with all drugs. There's a period right after you take it that if you draw a level, you don't know what you have got. You have to wait for it to be absorbed or get a bunch of points and you can draw a line through on a piece of log paper and

that will tell you what the half life is. And you can go back -- you can only go back in time to a point in time where your absorption is finished.

Q. If you were setting up an experiment to see response to various doses of digoxin in a person and all other things remained equal, weight, renal status, things of that nature, would you expect that person to respond differently at doses of point eight milligrams, point one zero milligrams, point one two five milligrams, point two five zero milligrams and then point five zero milligrams?

A. Did you mean point oh eight for the first dose? You said point eight.

Q. It would be eighty micrograms, a hundred mics, a hundred and twenty-five mics. Sometimes I mess it up.

A. The answer is yes. The short answer is yes and at some point you expect a therapeutic response and as you continue with the dose you would get other responses. In the real world what you do is you start a patient on a particular dose of Dig and you keep giving that dose until you get the plasma level to

stabilize. That's called digitalizing and that takes a few days and the reason is Dig has a long half life for up to a few days and it takes six to ten days to get up to the plasma level of digitalizing patients so after the first dose you typically don't see a complete therapeutic response. It takes some time to develop.

Q. You want to get them up to what's known as steady state, correct?

A. That's where they are going, yes, plateau.

Q. And do you know what the typical -- is it Cmax, what the peak is when you take it on a daily basis, that peak that comes when you have absorbed a drug. Is that what that's called, Cmax?

A. Yes.

Q. Do you know what the typical Cmax is for a hundred and twenty-five micrograms of digoxin?

A. The number?

Q. Yes.

A. No. I can look it up.

Q. I just want to know if you know.

A. Eight or ten. I don't know. Twenty.

Q. Are you talking about nanograms per milliliter?

A. Yes, I am.

Q. So it's your understanding that a typical hundred and twenty-five microgram dose would take somebody well beyond two nanograms per milliliter every day?

A. I said I don't know. I would have to look it up. You pressed and you wanted a number so I gave you a number. I don't know what the number is. It's higher than the therapeutic range and that's why you don't take the level for six hours.

Q. That's fine. If you don't know, you can just tell me you don't know. I don't want you to guess.

A. Thank you.

Q. Well, do you know whether in patients with normal renal function and not taking other meds that might interact with digoxin, whether their Cmax ever goes above two nanograms per milliliter?

A. Probably does, yes. That's why

you don't take it for six hours, it goes up and goes back down.

Q. What textbook or pharmacokinetic articles would you look to to determine the PK data on digoxin?

A. DRUGDEX, Goodman & Gilman. We just did that.

Q. So, for example, if Goodman & Gilman, if I looked back at those references that I read into the record, that might have some of that PK data.

A. It will, yes. That's what that chart is in the back.

Q. And so far as literature is concerned, you printed out and brought with you some research.

MR. MORIARTY: Can you mark this for me?

(Thereupon, Defendants' Exhibit 40-C, a group of documents from MICROMEDEX Healthcare Series labeled Cardiac Glycosides, was marked for purposes of identification.)

Q. Showing you what I've had marked as 40-C, is that material from your research file?

A. That's a printout from DRUGDEX, a database on Dig.

Q. And if it's okay with you I'm going to have the court reporter take that and make it part of the record. Do you need this original back or is a copy of it later going to suffice for you?

A. You can have it.

Q. And then is this one just about the antidote --

A. Yes.

Q. -- for extreme digoxin toxicity, Digibind?

A. Yes.

Q. And then what is this one from?

A. That's the section on digoxin from Goodman & Gilman, from the book in front of you there.

Q. Same edition?

A. Yes.

Q. And then inside this manila folder which was also part of your materials?

A. That's the DRUGDEX printout on digitalis, digoxin, cardiac glycoside.

Q. So the one I marked as 40-C just

says cardiac glycoside and is the one that's in this manila folder a subset of 40-C?

A. I think it's the other way. I think this is the summary and that's the unabridged (indicating).

Q. And is this -- are the contents of this manila folder just one continuous document?

A. It is.

Q. And it looks like it is eighty-nine pages long; is that correct?

A. Yes.

Q. And is it okay if I mark this one and then we can get you a copy back?

A. I don't need a copy back.

MR. MORIARTY: Let's make this 40-D.

(Thereupon, Defendants' Exhibit 40-D, a group of documents from MICROMEDEX Healthcare Series labeled digoxin, was marked for purposes of identification.)

Q. I've got all the original stuff down here on the floor so if you need to look at any of them, you let me know. Okay?

A. Yes, sir.

Q. The traditional doses now are a

hundred and twenty-five and two hundred and fifty micrograms; is that correct?

A. They are.

Q. Are you aware that there used to be a five hundred microgram dose routinely marketed by pharmaceutical companies and permitted by the FDA?

A. I don't know the answer to that question.

Q. Have you read any literature about the pharmacokinetics of digoxin five hundred micrograms?

A. I have no idea. Probably have. I don't know.

Q. Would you agree that the effect of -- I'm sorry, let me rephrase that. I want you to assume that there is a patient who was prescribed a hundred and twenty-five micrograms once a day of digoxin.

A. Yes.

Q. And they either intentionally or accidentally took two hundred and fifty micrograms a day?

A. Um-hum.

Q. Once, for one day, in other words.

Would the effect of that doubling of the dose for one day vary considerably from patient to patient?

MR. THOMPSON: Object to the form.

THE WITNESS: Well, yes and no. The yes part is the dose is doubled so an increased amount of drug would go to the receptors and cause the various kind of effects in the patient. Would different patients respond differently to too much drug, probably. Different weight, different medications, different, different, different, yeah.

Q. Would you agree there would likely be some patient who's got a double dose on whom it would have no adverse effects at all?

A. Probably not.

Q. What's the basis for that statement?

A. Well, the basis is the pharmacology of the drug, you're giving twice the dose that the patient should have in the first place and the only way you would know there were absolutely no adverse effects is if you were monitoring the patient and that's not likely to be the case so I think to assume that

it wouldn't have any adverse effect is not something that's supported by anything but somebody's armchair opinion.

Q. Maybe I didn't ask my question clearly. Are you saying that if a patient took a double dose once -- had been on steady state of point one two five and then suddenly took point two five zero once, are you saying every patient who did that would have adverse effects like digoxin toxicity?

A. What I'm saying they would have an increased amount of digoxin at the receptor and that their response to that drug would be different than it was with the point one two five. There's molecular thermodynamics involved here and when you give an increased dose you get an increased amount of drug at the receptor and the idea that that increased amount of drug binding the receptor doesn't cause any effect is really not a very tenable point of view.

Q. Okay. Well, I'm not suggesting that. I'm asking whether universally patients would have digoxin toxicity, the signs and symptoms of digoxin toxicity, adverse reaction?

A. Some would, some wouldn't.
Q. Again, that would be an individualized inquiry, correct?
A. No, every one of them is going to have more Dig binding to their receptors than they did at the lower dose. Every one of them, every single one of them.
Q. But it would be an individualized inquiry to find out if they had the clinical signs and symptoms of digoxin toxicity?
A. They could be monitored, yes. In the real world that doesn't happen.
MR. THOMPSON: Just a second.
(Pause in proceedings.)
Q. Let me ask you about post-mortem toxicology. Is that a subject you know much about?
A. Unfortunately.
Q. Do you agree that it has been known for many years that digoxin measurements in heart blood collected post-mortem may be misleading when attempting to assess peri-mortem plasma digoxin concentrations because of leakage of digoxin from heart muscle after death?

A. I'm aware people made statements like that. The whole business of necrokinetics is complex.

Q. Do you agree that the use of peripheral blood is no more reliable?

A. Blood from anywhere can have usefulness in figuring out a particular toxic case. Sometimes you get to know where it's from and sometimes it's of traumatic origin and sometimes it from the heart and sometimes it from the femoral vein and sometimes it's from places you don't know.

Q. All right. Well, in Baselt's text which you brought with you, in the digoxin section it says in part it has been determined that serum digoxin levels nearly always increase after death due to leaching from muscle. Do you agree with that?

A. Sometimes true, yes.

Q. I don't know if I asked you this before, but there was a big study about digoxin in the '90s called the DIG Trial. Have you ever read the papers that came out of the DIG, capital D, capital I, capital G, Trial?

A. Probably.

Q. In the DIG Trial, there were patients on placebos who were suspected and hospitalized of having digoxin toxicity. Do you have any idea why?

A. Well, they probably got worse. They probably got an arrhythmia or had confusion or other symptoms that can -- are common to Dig toxicity and have other causes. Each symptom gives us an index of suspicion and if you have somebody who has visual changes and confusion and arrhythmias, then that makes them a candidate for we need to evaluate for Dig toxicity.

Q. And, of course, coming into the hospital, no one knew whether they were on Dig or not, correct?

A. Yes.

Q. So they had to evaluate them, right?

A. Yes. And it sounds like an easy proposition to ask them are you on Dig but sometimes they get so confused they can't answer the question.

Q. Well, at least in the circumstances of the trial, they may not know,

right?

A. Or they may have been unconscious.

Q. Okay. Let's go to Exhibit 41. Do you have a copy of your report there? I've got extras here if you need it?

A. Let's see, this is 40 -- 41 is my CV.

Q. I'm sorry, 40 is your report.

A. Okay.

Q. Do you have a copy of it in front of you?

A. I do.

Q. And it's dated June 4th, 2010; is it not?

A. It is.

Q. And it is not paginated?

A. But the sections are numbered.

Q. I count eight pages.

A. Okay.

Q. Is that right?

A. I'll take your word for it, Counselor.

Q. And that's your signature on the last page, I assume?

A. It is, yeah. The reason the font

is different is that I signed it and scanned it in so I could send it electronically so they would have a copy of my signature on the document.

Q. All right. Now, I think I asked you this before, but you did not read Dr. Semigran's report?

A. No, I did not.

Q. Have you read any case specific reports in any of the Digitek lawsuits?

A. I don't think so, no.

Q. What I mean by that is there have been cardiologists hired in various specific cases to talk about specific patients.

A. No.

Q. You haven't seen those?

A. No.

Q. Now, Exhibit -- in this stack of materials that you reviewed, you can have this if you want -- there are yellow Post-it notes on here, are there not?

A. There are.

Q. And these correspond to exhibit numbers?

A. They do.

Q. So, for example, one of the things you had available to you was Exhibit 26; is that right? Well, I should start with 25. Somewhere in here I think you had 25?

A. Yeah, I did. I remember having Exhibit 25, the number on it.

Q. Well, here's the stack. We can get to it if we actually need it. I don't see any reference or discussion of Exhibit 25 in your report, Exhibit 40. Am I right about that?

A. Well, let me see what it is. Can you show it to me so I can figure out where it is here?

Q. Exhibit 25?

A. Yes. Here it is. I've got it. It's a warning letter from -- let's see -- looks like FDA to --

Q. To my client.

A. Divya Patel, president of Actavis Totowa dated February 1, 2007. Yes, I have it.

Q. The question I'm asking is I don't see any discussion of Exhibit 25 in your report itself. Am I correct about that?

A. I don't know the answer to that

question. I read it and this material is -- the letters from the FDA to the company are kind of a unit of information.

Q. They are background material, right?

A. They are.

Q. But my question is in your report, Exhibit 40, I don't actually see any discussion of Exhibit 25, any explicit reference to or discussion. Am I correct about that?

A. I don't know the answer to that question.

Q. Did you need to look at your Exhibit 40 to see if you refer to or discuss Exhibit 25 because when I read it I didn't see it.

A. It talks about quality control problems which eventuate in the letters relating to quality control. I didn't reference any of these documents specifically.

Q. Okay. So that would include -- the documents you didn't refer to or analyze in your report?

A. No, no, no, that's not what I'm saying, Counselor. I read these documents, I

looked at them and I wrote this report. It doesn't mean I didn't read them or that I disregarded them.

Q. You need to listen to my question.

A. I did.

Q. I don't see anywhere in your report where you specifically refer to or analyze the content of Exhibit 25 in your report.

A. Okay. You don't see that. Okay.

Q. Do you see it someplace that I don't?

A. I neither see it or don't see it. I don't have an opinion about that.

Q. All right. Do you specifically refer to or analyze the content of in your report Exhibit 26?

A. I don't know the answer to that question.

Q. What about Exhibit 50?

A. The answer is the same. I read these documents and I wrote the report.

Q. Would the answer be the same for Exhibit 68?

A. The answer is that I read these

documents and wrote this report.

Q. I understand that, but I need to go through them to make sure that your answer is the same for all of them.

A. It is.

Q. So 71, 79, 82, 106, 220, 221 and 229 and 234, you did not specifically refer to or analyze in your report itself, correct?

A. No. I have answered this question three times. I read these and I analyzed the content. You keep insisting on inserting the word that I didn't analyze these reports. I analyzed these reports.

Q. This is pretty simple. I don't know why we're miscommunicating here.

A. It's pretty simple because what you want me to say is I didn't analyze anything in these reports and I'm not going to say that because I did.

Q. That's not what I'm saying. You read them, didn't you?

A. I did.

Q. You reviewed them?

A. Yes.

Q. And you probably analyzed them?

A. Yes.
Q. But you don't refer to them or specifically write anything about them in Exhibit 40, do you?
A. Yes, I do. I talk about misbranding and I talk about adulteration and those topics are covered in these reports.
Q. Show me exactly where you're referring to in your report, Exhibit 40.
A. Well, those two statements are in these documents.
Q. Those words are in those documents, right?
A. They are.
Q. And --
A. That's how they got into this report. They got into this report from these documents as a result of my reading it and analyzing it.
Q. So --
A. So, no, I'm not going to say I didn't analyze the reports.
Q. So in your report, Exhibit 40, in Roman numeral II on the first page, you say I am familiar with the FDA rules and regulations

with respect to misbranding and adulteration by education and experience as well as licensure as a registered pharmacist in Ohio and Minnesota?

A. Yes.

Q. Do you talk about adulteration and misbranding anywhere else in Exhibit 40?

A. I talk about being unable to rely on the contents of Digitek tablets which is the same issue.

Q. And where is that?

A. On section 9, too much Dig, too little Dig.

Q. Are you talking about Roman numeral IX?

A. I am. And in clinical applications and in dosing.

Q. Okay. Is that it?

A. And in summary.

Q. On the last page, correct, page eight?

A. It's the next to the last page.

Q. Anywhere else in your report that you didn't mention?

A. There may be. I don't know.

Q. Now, also shown to you and sent to you was the report of a Dr. Tallarida; is that correct?

A. Yes.

Q. And I didn't see anywhere in your report where you discuss Dr. Tallarida's report; is that correct?

A. That is correct.

MR. MORIARTY: Can you mark this as 40 -- I think we're up to E.

(Thereupon, Defendants' Exhibit 40-E, a one-page document entitled Response to Defense Pharmacologist Expert Report, was marked for purposes of identification.)

Q. Showing you what I've had marked as Exhibit 40-E, it's a document from your files. Do you recognize it?

A. I do.

Q. Did you type it?

A. I did.

Q. Does it contain your comments regarding the Tallarida report?

A. It does.

Q. Did you send this document or convey the contents of it to anybody at

Mr. Thompson's office?

A. No. Those are my notes about that expert's report.

Q. Do you have this in your computer at the office?

A. I don't know where that is.

Q. I'm going to keep it with the exhibits and if you need a hard copy back, we can arrange to do that and it will be with the transcript. Is that acceptable to you?

A. Yeah. I need a copy of it back.

Q. Do you need a copy of it today?

A. Well, if you're going to ask questions about it, I do.

Q. I'm not going to ask questions.

MR. THOMPSON: Let me interrupt just very briefly. Dr. Nelson, in fact, showed that document to me last night and that was the first I had seen it, but I think he was excluding the meeting that we had last night from his answer.

Q. In any of these exhibits that were sent to you, the ones we were just talking about and that I enumerated, did you see any actual USP or comparable testing of Digitek tablets indicating that those tested tablets

were out of specification?

A. No.

Q. Do you know doctor -- or do you know professor or Dr. Tallarida, by any chance?

A. I do not. Sounds like an interesting fellow.

Q. All right. Let's get back to Exhibit 40. The very first paragraph under Roman numeral I after it lists what you reviewed by exhibit number, it says I have also relied upon standard texts called references. Did you look at any other textbooks beside the Baselt and Goodman & Gilman texts that you brought with you today?

A. I probably did. This case started in 2008. I have undoubtedly read a number of textbooks between 2008 and 2010.

Q. And do you know what additional textbooks you looked at?

A. I can't cite chapter and verse, no.

Q. Which ones would you typically look at for this kind of reference?

A. I don't have any textbooks to cite.

Q. Let's go to Roman numeral IV which has the caption ancient use.
A. Yes.
Q. You use the word poisoning?
A. Um-hum.
Q. You see that?
A. Yes.
Q. And I would assume that in general poisoning occurs when somebody takes too much of a particular substance?
A. Yes, it does.
Q. Is that true?
A. In pharmacology it occurs when they take the right dose.
Q. Do you agree with -- since we're into ancient use category here, do you agree with the quote attributed to Paracelsus that the dose makes the poison?
A. I do.
Q. What does that actually mean to you?
A. Well, all of pharmacology is a partial poisoning. If we discover a new toxin or poison in nature, pharmacologists take it back to the laboratory and study it to see how

it works, and if that mechanism of, quote, toxicity has a therapeutic application and sometimes that pans out and we end up with a new medicine so all pharmacology is a partial poisoning of something.

Q. But what I mean is what is the dose makes the poison? What's the dose issue? I mean, is everything toxic if you take too much of it?

A. Yes.

Q. People can die from drinking too much water, I assume, right?

A. Yes, in fact they do. It's amazing.

Q. Let's go to VIII, Roman numeral VIII D.

A. Okay.

Q. Is says elimination. Under normal conditions the renal excretion of digoxin is slow with about half of a given dose excreted in two days. Do you see that?

A. Yes, sir.

Q. Is that in normal renal function?

A. Yes.

Q. And then you refer to Digibind in

the second paragraph of D, do you not?

A. I do, yes.

Q. And do you know in what percentage of digoxin toxicity cases Digibind is prescribed?

A. It's only in severe cases. If a judgment is made that the patient is likely to survive their overdose, the patient may be hospitalized and monitored. Digibind is of use primarily in large overdoses where there is life-threatening toxicity that's the setting that it's typically used in as opposed to somebody gradually becomes chronically toxic. In that kind of a situation if they are clinically stable they are usually hospitalized and monitored and the drug is stopped and time is allowed to pass for the excretion of the drug.

Q. Okay. Now, under Roman numeral IX --

A. Yes.

Q. -- the ADME balance, what does ADME actually stand for.

A. It's in the previous page we start with absorption, distribution, metabolism and

elimination. Those are the four cornerstones of pharmacokinetics. In other words, what the body does to the drug.

Q. And in the last sentence of Roman numeral IX, section A, it says the toxic effects of digoxin include nausea, vomiting, cardiac arrhythmia, slow heart rate, confusion, dizziness, heart block and death.

A. Yes.

Q. Would you agree that typically a patient who becomes digoxin toxic goes through a progression of these symptoms from the mildest ones first?

A. No.

Q. You wouldn't agree that that's what typically occurs?

A. No.

Q. All right. In what percentage of cases is sudden death the outcome of digoxin toxicity?

A. I don't know the percentage, but it happens and the problem with toxicity is that sometimes it goes in the progression as you've alluded, and other times you get sudden death.

Q. Well, do you know the percentage of which it occurs?

A. I don't know a number, but I know it happens often enough that if you have got an overdose you need to be ready to respond quickly if there's heart block and arrhythmias which can be fatal in a matter of minutes.

Q. Well, is it --

A. You can't wait for this, A is going to happen, B is going to happen and we've got plenty of time and C is going to happen. Sometimes the patient crashes and dies quickly without developing any of these other milder symptoms so the idea that the milder symptoms always precede death is not true.

Q. I'm not asking you if they always precede death.

A. Usually they do, yes, not always.

Q. Usually. In the majority of cases they do, correct?

A. Yes.

Q. Do you know what the source -- I'm sorry, I've moved up to Roman numeral section X, the top of the next page. You say digoxin is a drug with a very low therapeutic index in

the range of two to five. Do you know what the source is for your statement that it's in the range of two to five?

A. There is not one specific reference to that. Various numbers are given. Some sources say two, some people say five. The idea -- the therapeutic index is not an absolute number. You don't go to a reference and look up the therapeutic index. It's a range and the range is two to five. The idea is that if you give twice the dose that a person responds to, you're likely to get into serious toxicity. If you give five times the dose, you're going to have a higher probability of getting into serious toxicity.

Q. Let's go to Roman numeral XII, and you're talking about each dose of digoxin is patient specific. You still agree with that, correct?

A. Which line is that in?

Q. It's right in the middle of the paragraph.

A. Each dose of digoxin is patient specific, yes. Um-hum.

Q. And then you're talking in the

last sentence about adjusting the dose based on clinical response.

A. Um-hum.

Q. Do you see that?

A. Yes.

Q. And some of the things that the clinicians, prescribers and other doctors taking care of the patient would assess include EKG, blood pressure, heart rate, urine output, edema, exercise tolerance, lab tests, side-effects. Those are some of the ones you mentioned, correct?

A. Yes.

Q. And that would include renal status, if necessary?

A. Yes.

Q. And would that include also the serum digoxin concentration if appropriate?

A. It's done sometimes. It's not done always. It's probably not done as often as it should but it might be useful in that setting, yes.

Q. Now, in Roman numeral XIII, you're talking about tablets that are outside the USP specs are adulterated and misbranded, correct?

A. Yes.
Q. And the type of tablets you're talking about that would be worse than nothing is if they in fact are outside the USP specs, correct?
A. Yes.
Q. You're not talking about tablets that, for example, have the wrong color, but did not affect the dose; is that right?
A. I don't know. Wrong color might be a problem. The patient sees the tablet is not the right color, doesn't take it, goes into failure and dies. That could be trouble, yeah.
Q. That's not what I'm talking about. I'm just talking about if the tablet was for some reason yellow but was supposed to be white, but the active ingredients were all within the USP specs, then they wouldn't necessarily be dangerous, correct?
A. I don't know.
Q. Well, do you know --
A. That seems like a very theoretical question that I don't have any data about, I'm not an expert about and don't have any answer to.

Q. Well, do you know whether tablets that were the wrong color but nothing else was wrong with them would be considered adulterated and misbranded by the FDA?

A. Yeah, they would. They are supposed to be the color they are supposed to be.

Q. Let's go to Roman numeral XIV.

A. Okay.

Q. It's entitled digoxin toxicity, correct?

A. That's correct.

Q. And in the first sentence you say the symptoms of digoxin toxicity are not pathognomonic of toxicity, then you go on?

A. Um-hum.

Q. How are you using pathognomonic in this context?

A. Well, pathognomonic means if you have that symptom, you have got the diagnosis. What it means in this sentence is delirium and confusion are not unique to digitalis.

Q. Are you done with your answer? I don't want to cut you off.

A. That's an explanation of the

question, I think.

Q. Sure. Have you ever heard the phrase signature disease?

A. Signature disease?

Q. For example, sometimes somebody would say mesothelioma is a signature disease for asbestos. Have you ever heard that?

A. I haven't, and there are other causes of mesothelioma, so I don't even think it's true.

Q. If I understand what you are saying in the first sentence here is that the signs and symptoms of digoxin toxicity can be vague in the sense that they look like other problems, right?

A. Each one is nonspecific. Obviously if you have nausea, it might be the flu, it might be Dig toxicity. If you have blurred vision, it might be glaucoma, it might be Dig toxicity.

Q. It could be from another drug?

A. Sure. And what I go on to say is that the more of these you have, if you have this and this and this and this and you have five of these, the probability increases that's

what it is. In other words, if you have visual disturbances and cardiac arrhythmias and so forth, the probability that it's digitalis toxicity increases and in the real world of clinical medicine and clinical toxicology, these signs and symptoms are used to make a presumptive diagnosis of digitalis -- Dig intoxication.

Q. All right. So if we go to the next page to the second full paragraph on that page, while a high serum digoxin finding by lab test is useful -- do you see that?

A. Yes.

Q. Are you saying there that somebody could make a diagnosis of digoxin toxicity even if the lab result was within the therapeutic range?

A. Yes.

Q. So let go to the last paragraph in that section and you're talking about how the diagnosis will depend on a myriad of factors, right?

A. Yes. And there's a typo right after factors. Look at that. I'll tell you what.

Q. What's it supposed to say?
A. There's not supposed to be a minus sign there.
Q. I just thought it was a good old-fashioned dash.
A. Okay, we'll take it as that, Counselor.
Q. And then you say thus, whether an overdose of digoxin has produced symptoms in a specific patient must be ascertained by the patient's physician with reference to the specific facts, signs, symptoms, lab findings and monitoring data from the specific patient; is that correct?
A. Yes, sir.
Q. And that treating physician is in the best position to do that, aren't they?
A. Well, they can be. A clinical toxicologist, cardiologist might do a better job on referral, but, yes, usually it's the attending physician.
Q. Well, I'm not excluding consultant -- contemporaneous consultants, but the medical providers on the scene dealing with this in what they call real time are in the

best position to assess this, aren't they?

A. Yes.

MR. MORIARTY: All right. Why don't we take a five minute break. I need to talk to Ericka.

(Recess held.)

Q. You brought with you a manila folder with a report dated June 3rd, two -- it actually says 1010 but it was 2010, correct?

A. I don't know. I would have to look at it and see.

Q. (Indicating.) You're not suggesting you were alive a thousand years ago to write this for me?

A. I don't think so.

Q. You are pharmacologically well preserved.

A. Yeah.

Q. So there were drafts before you signed and finalized Exhibit 40, correct?

A. Yes. That's a draft.

Q. And did you write these yourself even?

A. Did I write them, yes, I wrote them myself.

Q. Did you have some discussions with counsel before they were finalized?

A. I had a telephone conversation in the process of finalizing the report and some typographical errors were called to my attention, which I fixed.

Q. Okay. Now, let's go back to --

A. I fixed them all but the one. That's a dash that's there, but nonetheless --

Q. Let's go back to Exhibit 40, the final version, and let's go to the last page. Let me read this and ask you some questions about it. It says Digitek tablets can be very dangerous if they do not have a consistent dosage within the USP specification for the prescribed dosage. Did I read that correctly?

A. Yes.

Q. Now, I think what you're referring to is that if they are less than the labeled specifications, the patient could be subtherapeutic, correct?

A. Yep -- yes.

Q. And if the patient is sufficiently subtherapeutic could have problems related to the underlying disease for which they are

taking the medication like atrial fibrillation or congestive heart failure, correct?

A. Yes, sir.

Q. Because if it's subtherapeutic it may not actually be treating that disease, right?

A. Yes.

Q. And if the tablets have a consistently high dosage, the patient could develop digoxin toxicity, correct?

A. Yes.

Q. Have you read any medical studies of the tablets themselves, of a group of tablets themselves which indicated that the tablets were in fact outside the specifications, high or low?

A. There are two answers to that question. One is that there are documents indicating that there were double tablets which would indicate that there was twice the dose. The other answer is that there were faulty assurance problems with manufacture which resulted in the manufacturers being unable to document that the contents were within USP specifications.

Q. What I'm asking you about is not FDA documents, I'm asking you about scientific testing of the tablets themselves, okay? Not weight, not size. Whether there was -- whether you have seen any documents, scientific testing of tablets themselves that were outside of the specifications, either high or low?

A. I answered with what I know.

Q. So I assume the answer is no, you have not seen scientific studies of tablets themselves, correct?

A. I'm not sure if the documents regarding the double tablets rise to your level of scientific documentation. My understanding is that there is some evidence that they existed at one point and I've seen reports to that effect.

Q. Are you referring to the batch 70924A in which twenty double thick tablets out of a batch of 4.8 million were detected at the plant prior to shipment to market?

A. I believe so, yes.

Q. In your own practice as a pharmacologist, do you ever commission tests of pharmaceutical products to check whether they

are within or not within the specification?
A. I do.
Q. How often do you do that?
A. I don't know. A few times a year.
Q. What mechanism do you go through to do that?
A. I typically send them to an analytical laboratory.
Q. You secure some samples from a patient first, correct?
A. Yes.
Q. And then you send them to -- what analytical laboratory would you typically use?
A. Trying to think of the name. I'm sorry, my brain is a little --
Q. Only one I can think of off the top of my head --
A. National Medical Services, NMS Laboratories.
Q. Near Philadelphia?
A. They are in Pennsylvania somewhere, yes. I always have to go on-line and get the address. They are one of the few analytical laboratories still doing that kind of work. Sometimes there are other

laboratories available depending on the case. DEA Laboratories are criminal laboratories, but they have to have some interest in the case.

Q. And in your dealings with at least NMS, they have been responsible and in your view reliable?

A. They have, yes.

Q. So that is what you would do if you personally wanted to assess this subject yourself, correct?

A. Yes, that's one of the things that I would do given the number of tablets involved, one would need to have a statistical way of sampling and visualizing. Obviously, it's not practical to run a hundred dollar a pop test on how many million tablets are involved in this case, so -- but analyzing the content of an adequate sample and I would defer to a statistician about what an adequate sample would consist of, given the number of tablets involved here.

Q. And as time today marches on, and I can't remember what I asked you two or three hours ago, it's my memory that you have not done that with digoxin or Digitek specifically

recently, correct?

A. That is a true statement, yes.

Q. So I would assume that the question of whether there were in fact Digitek tablets outside the USP specifications is a subject you will leave to other experts in the case?

A. My opinion is that when a pharmaceutical manufacturer manufactures tablets, that the manufacturer has an obligation to assure the consumers of the product that the product is within USP specifications. If they can't do that, due to the health implications of tablets being out of specification, that the assumption is that tablets are not in specification rather than the usual scientific assumption which is the null hypothesis which says if you can't prove it, it ain't so.

Q. That was a lot to absorb so I may have to have her read part of that back. Where in any FDA reg does it indicate that the assurance has to be that the tablets are in fact within the specifications?

A. I think that's the whole point of

the FDA regulations, that it is so important that that be the case, that if you can't prove it, then it is not true.

Q. Are you saying that the company is supposed to prove that all the tablets are within the specifications?

A. They are supposed to do an adequate sample of their output and analyze them in an accepted manner to assure that it's reasonable that the output of the company is within USP specifications. Obviously you cannot analyze every tablet and this company didn't do that, certainly, no company does, and they didn't do adequate quality control to prove to anyone that the tablets are in specification. That's the problem.

Q. Have you read any batch records from the making of Digitek?

A. No, nothing recent.

Q. Have you seen any quality control testing of Digitek products?

A. No.

Q. Have you seen any quality assurance measurements of weight or thickness that were done during the manufacturing

process?

A. No.

Q. Have you ever seen any testing documents that were done by laboratories outside Actavis --

A. No.

Q. -- regarding Digitek?

A. No.

Q. Do you have any knowledge of whether FDA, any outside lab or even Actavis found out of specification Digitek in the years 2005 to 2008?

A. Other than the double tablets, no.

Q. So if I understand what you're really talking about, it's the adulteration standards that you referred to on page one of your report, correct?

A. The issue is of the tablets in the recall, can the manufacturer assure patients, physicians and pharmacists that those tablets are within USP specifications, and the short answer to that question is no and the implication that the public is protected because there are not enough analyses is in my opinion not a useful approach to the problem.

This is not the typical scientific evidentiary issue. It has to do with public health.

Q. What I want to know is where in the FDA regs it says anywhere that the burden is on the company to assure that the tablets are in fact within the specifications?

A. That's the whole purpose of quality control.

Q. No, I'm asking where in the regs that is.

A. There are quality control procedures which are to be observed which were not observed in this case.

Q. Can you cite to me a single FDA reg that puts the burden on the company to assure that the tablets are in fact within the specifications?

A. Yes. They have a -- there's a label on the bottle and the bottle says it contains point two five. If the company cannot assure to a reasonable extent that that's the case, then that's not the case. And that is the situation in this case.

Q. So you'd agree that the company certainly cannot test them all, correct?

A. There is no expectation that they do. The expectation is that they do reasonable quality control, which they did not do.

Q. Well, with all due respect you have not seen any of the actual quality control documents?

A. I accept the opinion of the FDA.

Q. Okay. Did the FDA -- have you seen a single document in which the FDA said that Digitek tablets were outside the specifications of the label according to the USP?

A. Yeah, they can't be sold as such because they are adulterated and mislabeled.

Q. I want to see whatever document you're seeing in your materials that says from the FDA that the tablets were actually outside the specifications?

A. That's what that means.

Q. You're equating adulteration with outside the USP specs?

A. Yes.

Q. Where in the definition of adulteration does it say that?

A. If there is not quality control to

prove that it is within the spec, then it is assumed to be out of spec.

Q. I'm just asking you where in the statute or the regs can you find me in your materials --

A. I'm not going to quote chapter and verse. It's the intent of the rules and regulations to assure the public has reliable pharmaceutical products.

Q. Well, the FDA doesn't expect a manufacturer to test a hundred percent of the tablets, do they?

A. I didn't say they did.

Q. And the FDA certainly because it approves the manufacturing and testing methods knows how many of the tablets get tested because they approve that system, correct?

A. They inspect it and supervise it, yes. And it is part of good manufacturing processes that would be quality control.

Q. Just so we can close this loop, it's your understanding that the adulteration statute itself refers specifically to the company assuring that tablets are within the USP specs; is that right?

A. Yes.
Q. And if you are mistaken and either the statute or the reg don't say that, would it change your opinion?
A. No.
Q. Do you believe that any product that is considered adulterated by the FDA is per se outside its USP specifications?
A. Yes.
MR. MORIARTY: I'm going to pass the witness to Ms. Downie.
THE WITNESS: Very good.
CROSS-EXAMINATION
BY MS. DOWNIE:
Q. How are you?
A. Good afternoon.
Q. I have a few questions for you in follow-up. Mainly clarification as well.
A. Very good.
Q. We will be skipping around a bit, but hopefully won't be too confusing. I believe you mentioned earlier when we were discussing some of your experience with diagnosing or evaluating digoxin toxicity that you had actually seen a case of it about a week

ago?

A. I evaluated a case about a week ago, yes.

Q. Can you tell me more about the circumstances of that evaluation?

A. It was a forensic evaluation in which the issue was the interpretation of a blood level of digoxin.

Q. And when you say it was a forensic evaluation --

A. Yes.

Q. -- does that mean it was done at the request of an attorney?

A. It was.

Q. Would that have been for the plaintiff's attorney?

A. Yes.

Q. And was that in the context of what we are typically referring to as the Digitek litigation or was it a different type of case?

A. It was a different type of case. It was involving the intravenous use of digitalis.

Q. Was it a medical malpractice case?

A. Yes.
Q. And who was the attorney that requested you make that review and evaluation?
A. It was Peter Miller.
Q. Okay. And have you -- you obviously have not prepared a report in that case or --
A. I didn't. Actually, one of the other faculty at the drug and poison center was handling the case and I was asked some questions about it.
Q. When was the last time you recall seeing a digoxin toxicity case clinically in your practice?
A. I don't know the answer to that question. We meet every week and discuss lots of cases. I don't know when it was a digitalis case was discussed. I don't know.
Q. And when you say we, you're talking about the poison center?
A. Yes. Every Tuesday we sit down and go over every serious overdose case for the past week.
Q. Does the poison center keep records of digoxin overdose cases or toxicity?

A. We keep records of calls that come into the Drug & Poison Information Center, yes.

Q. Do you also keep record of what -- and maybe I'm making an assumption. I'm sort of envisioning you get a phone call saying we think we have got a problem with toxicity or poisoning and you determine whether or not there is any poisoning or toxicity?

A. Yes. Most of the time we know what the drug is or we think we know what the drug is and we're trying to match up the symptoms with the history. And the symptoms are what we get and the history is what we get -- sometimes we get a good history, sometimes we get somebody's guess about what happened.

Q. And I think Mr. Moriarty asked you previously whether or not you had looked back at the center's records to determine whether or not there were spikes or peaks or anything of that nature.

A. Yes.

Q. And your response was you had not. But if you wanted to, could you provide that data or could you do that type of

investigation?

A. The data is going to be varied, I think. We have a massive computer and IT department and the data is in there someplace.

Q. And I apologize, I may be going over stuff you have already testified about. I understand you have -- your position, your academic position as well as your position at the center, and I believe at one point you testified that you also consulted with hospitals in certain cases when you're requested?

A. Yes.

Q. When was the last time you were requested to consult for a hospital on clinical treatment of a patient?

A. I don't know. A couple months ago, I guess, something like that, methadone overdose. That's the last one I can recall.

Q. And actually going through your CV it struck me that appears like that your main research interests over time has been some substance abuse and maybe some pain management as well. Would that be a fair characterization?

A. I spend a lot of time in that area. It's not the only thing that I do nor is it the only thing I'm certified to do nor is it the only thing I'm asked questions about and respond to in the normal course of my duties.

Q. Nor did I suggest any of that but I appreciate that. Have you ever done any specific research regarding digoxin?

A. Could you be more specific? You mean clinical research on patients?

Q. Any research, any published research other than what you already talked about?

A. No, my publications are in my CV. We've gone over that.

Q. So there's nothing else. There would be no other research you have done regarding digoxin that was not published or not in your CV?

A. Well, I'm not sure of the answer to that question.

Q. And why is that?

A. Well, my life has been complex. There may be -- there may have been situations where we looked into a case and gathered data

and so forth about it and I don't know how to answer that question.

Q. But in preparing for your testimony today and in preparing your report in this litigation, there's no research of your own that you went back to reference regarding digoxin; is that correct?

A. Yes, I think that's correct.

Q. Have you ever focused in any respect with respect to regarding cardiac medications in general?

A. I'm thinking. Probably, yes. When I was doing contract pharmaceutical work we had clinical trials that involved cardiovascular diseases, hypertension, use of diuretics and so forth.

Q. When was that?

A. Those were phase two clinical trials.

Q. And when was that?

A. Those would be in the '80s.

Q. Since then?

A. Not that I can think of off the top of my head.

Q. And, again, I apologize,

Mr. Moriarty may have already asked you this, but have you consulted with the FDA at any time directly?

A. I don't think so.

Q. The digoxin overdose case that you consulted on about a week ago, that was intravenous digoxin?

A. Yes.

Q. Do you consider there's a difference between overdose and toxicity definitionally?

MR. MORIARTY: Overdose and what?

MS. DOWNIE: Toxicity.

THE WITNESS: Well, they are different words. Overdose is kind of a street term, I guess and toxicity is more specific to receiving too much of a drug or chemical.

Q. When you have been using the terms in this deposition today, when you have used the terms overdose and toxicity, have you meant them to mean the same thing or something different, just so I'm clear?

A. When I say overdose, I mean for some reason the patient got too much. Toxicity is what happens to the patient after you give

them too much. So the overdose is grandma accidently ate ten tablets, the toxicity is she has cardiac arrhythmias.

Q. But can you also have toxicity without overdose?

A. It's possible.

Q. As I understand it, the poison center you're affiliated with, you receive phone calls from the public regarding drugs and questions that they have. Do you also receive phone calls from physicians and healthcare providers?

A. Yes.

Q. Do you have a call center that takes those calls?

A. We do.

Q. Are you involved at all with working with the call center to monitor the type of calls that they are getting?

A. Yes.

Q. And you mentioned that you have weekly meetings?

A. Yes.

Q. And in those weekly meetings, do you talk about some of the calls that you're

getting to determine whether or not there's any trend or information that you need to be particularly aware of?

A. Yes.

Q. And I know you said you have not done a study of the poison control or poison center's data regarding calls that they have gotten, but do you specifically recall at any time discussing with any individuals from the call center or during the weekly meetings there was a rise in calls regarding digoxin toxicity?

A. I don't recall a rise in calls. There may or may not have been and to be forthright, many times when there is publications in the media of a recall or an issue with a medication, the number of calls will go up as a result of that as opposed to what we might first think of as, you know, the number of overdoses from it. And the short answer is I'm not aware of either of those things going on.

Q. And when is the first time you recall learning about the recall for Digitek?

A. I think it was 2008.

Q. Do you recall how you came to

learn that information?

A. I think I became aware of it from Teresa Toriseva because at that time I wasn't receiving electronic notifications of recalls.

Q. Why is that? Had you been receiving electronic notifications of recalls for a period of time?

A. More recently I have, yes.

Q. Since when?

A. For about a year or so, something like that.

Q. Is there a particular reason you began receiving electronic notification of recalls?

A. I subscribed to an electronic database that notifies people who are interested in pharmaceuticals about recalls. I particularly became interested with Baxter's problem with the heparin recall. It was a very upsetting event to me so I wanted to follow other recalls and so I subscribed to a database that informed me about those things.

Q. So would it be fair to say that prior to a year -- prior to a year ago, you weren't regularly following FDA recalls?

A. No. We get information from all kind of sources at the center about recalls and I was aware of lots of recalls before last year.

Q. Right, but you weren't aware of the Digitek recall until you spoke to Ms. Toriseva?

A. Yes, I think that's a true statement.

Q. You worked as a pharmacist from approximately 1972 to 1973; is that right?

A. No.

Q. No?

A. I've been a pharmacist all my life.

Q. Practicing pharmacist?

A. I started practicing in 1970 and it's 2010 and I'm still practicing.

Q. I understand what you're saying, but you were talking I guess at some point about experience you had in 1972, 1973. Why don't you just tell me what you were doing in those years and maybe it will refresh my memory.

A. Well, when I first got out of

school, it was June of 1970 and I worked in a retail pharmacy in Merced, California until November of 1970, at which time I went to the University of Minnesota College of Pharmacy and College of Medicine and ran the outpatient pharmacy from November of 1972 to -- no, November of 1970 to June of 1972 at which time I came to the University of Cincinnati College of Medicine and The Drug & Poison Information Center, and at some times during my early years in Cincinnati, I spent some time in a dispensing pharmacy moonlighting and the -- my responsibilities at The Drug & Poison Information Center require that I continue to maintain my pharmacy licenses which I've done. And the boards of pharmacy think of providing poison control services as practicing pharmacy.

Q. Okay. If a medication is found to be by the FDA adulterated, is that medication recalled from the market?

A. Should be, yes.

Q. Is it? What are the FDA regulations with that?

A. My assumption is that --

Q. Let me just stop you. I don't

mean to cut you off, but I just want to know if you know what they are or not.

A. I do not know the chapter and verse of the FDA regulations regarding that issue.

Q. I certainly don't expect you to recite them word for word. Why don't you just give me a synopsis.

A. My understanding if the FDA determines that a drug is misbranded or adulterated, it needs to be removed from commerce.

Q. In all cases?

A. In all cases, yes.

Q. You were talking to Mr. Moriarty about drug interactions with digoxin at one point.

A. Yes.

Q. And it appeared that the only source that you found to be reliable other than going directly to specific literature sources would be DRUGDEX, I think is what you referenced.

A. Yes.

Q. Can you -- DRUGDEX. Spell dex for

me so I know --

A. D R U G D E X.

Q. Is there any other source other than that source that you find reliable with respect to drug interactions or is that the only one?

A. My experience tells me that it is the most reliable among the resources that are out there so I use it. There's a lot of garbage in the drug information literature and it's abundantly available online and other places. It's a tough literature to evaluate and that's why I use DRUGDEX.

Q. Well, you're a professor, you're teaching students who are going to ultimately go out --

A. I'm treating patients whose lives depend on my advice and I don't want to go to some reference that's got some misinformation in it that's been copied and copied and copied and copied and is incorrect. And if you use other systems, I run into that problem.

Q. So is that the system that you're teaching your students they should use in their practice?

A. That's correct. In fact --
Q. Is that the system that you would instruct physicians to utilize --
A. Absolutely. All my medical students must memorize the number of the National Poison Control Center, and if they do so they get three points on their final examination in pharmacology. That's how important it is to get it right.
Q. Three points out of how many?
A. A hundred. Puts some over the top.
Q. You were testifying earlier that anything above two increases the probability of toxicity?
A. Yes, digoxin above two nanograms per mil, yes.
Q. At what rate does it increase that probability?
A. It's in the reference that I supplied from Gilman & Goodman that we went over earlier.
Q. I specifically want to know if you can tell me as a layperson how much it's going to increase that probability once I get above

two, for example, how much will it increase the probability when I go from two to 2.5.

A. It's in the reference. When you get at a high number it's ninety percent.

Q. Can you tell me if you look at it?

A. Yeah.

MR. MORIARTY: I put your books back down over there (indicating).

THE WITNESS: Okay.

Q. And I'm sorry.

A. This is Goodman & Gilman's 10th edition, page 1949. Mean data following oral dose. Patients with congestive heart failure who exhibited no signs of digitalis toxicity. No signs of toxicity respectively. Quote, concentrations above point eight nanogram per mil were associated with high neutropic effect. Concentrations of 1.7, 2.5 and 3.3 nanograms per mil were associated with ten percent, fifty percent and ninety percent probability of digoxin-induced arrhythmias. So the more you have, the worse it is, like I said.

Q. Is there any other sources that you relied on other than that one?

A. No, that's it. That's the Bible.

Q. So when you're talking about toxicity and it's talking about digoxin-related arrhythmias, you're using those terms interchangeably?

A. Yes. Digoxin-caused arrhythmias is a digoxin toxicity.

Q. Can you have digoxin toxicities without digoxin-caused arrhythmias?

A. It's possible. Not likely.

Q. So in most cases you would expect to see digoxin-caused arrhythmias in the cases of digoxin toxicity?

A. Digoxin acts on the heart. The more digoxin you have -- if you have too much of it, the more likely you are to have arrhythmia, yes.

Q. Just so I'm clear, I'm not trying to be difficult. I just want to understand your answer.

A. My answer is the higher the serum level is after two, the more likely you are to have digitalis toxicity.

Q. But my question is are you saying more likely than not in most cases you will see digoxin-caused arrhythmias in cases of digoxin

toxicity?

A. No. What I'm saying is digoxin-induced arrhythmias are one symptom of digoxin toxicity. I'm not saying that they are the first symptom in fifty percent of the cases which is more likely than not. What I'm saying is the higher the level, the more likely you are to have arrhythmias. Arrhythmias is one of the symptoms of toxicity. It happens to be one of the more serious symptoms of toxicity and it's a symptom of toxicity that kills people so it's a symptom of toxicity that we're interested in as toxicologists, and it correlates with the serum level of digoxin.

Q. So you are saying you're only going to have digoxin-caused arrhythmias in cases where the serum levels are higher?

A. No, you can have it in normal levels. It just doesn't happen as often.

Q. What do you mean normal level?

A. Within a therapeutic range of one to two. You can have a normal digoxin level and arrhythmias. You're more likely to have arrhythmias as the blood level goes up and that's what the data says and that's what I've

been saying.

Q. Was it your testimony earlier if you recall that anything above two is toxic?

A. It's more likely to be, yes.

Q. And was it also your testimony that every day an individual reaches a peak level that would be above two?

A. Typically they do, yes.

Q. So every day people are generally in the toxic range?

A. No.

Q. No? Why not? Then I misunderstood what you said.

A. Well, pharmacokinetics is not simple. Okay? What happens is in time zero you take the drug and the drug level in the blood goes up. The drug is just there, it's in the blood. And then in about six hours it comes down to its plateau. So if you measure the amount in the blood when it's being absorbed, it's really high and if you don't know the difference between a trough level and a peak level, you can say yeah, it's over the moon, the patient is toxic.

If you understand complex science,

pharmacokinetics, pharmacodynamics and toxicology, you will say well, the level doesn't count until it's down to its plateau level. Why doesn't it count? The answer to why doesn't it count is that the drug is going through its distribution phase and it's distributing to the rest of the body and it is distributing to muscles, including the heart muscle, and so a useful digoxin level is one obtained at least six hours after you give the tablet, and what's happening in the middle is the absorption and distribution phase.

Q. Okay. But that highlights why it's important to take that serum digoxin level at the appropriate time in order to get an accurate picture of what that level is?

A. And it happens to be true in every other pharmaceutical. It's a general principle of pharmacokinetics that can't just take the level thirty minutes after you give the drug and we don't ever do that. People that know what they are doing don't do that. Let's put it that way.

Q. Bear with me.

A. Okay.

Q. How many cases, if you can tell, have you investigated or been involved with in which digoxin was the cause of sudden death?

A. I don't know. Several, I'm sure, over the years.

Q. Sounds fairly dramatic to me. I would think you might recall the circumstances of those. Do you?

A. Not necessarily. There are digoxin deaths every year from overdoses.

Q. Were they digoxin overdose cases where somebody ingested too much of the drug?

A. Yes, typically they are. Some are suicidal, some are homicidal, some are accidental in pediatrics. Those are the kinds of overdose cases we see.

Q. Are you talking in general or about digoxin?

A. I'm talking about digoxin and I'm talking about overdoses in general, those are the settings we see, pediatrics, accidental, suicidal and homicidal.

MS. DOWNIE: Give me just a few more minutes to review.

(Pause in proceedings.)

Q. Did you review any documents from the FDA regarding Digitek other than the documents that were in your file?
A. No.
Q. Is it your testimony that you believe that the FDA found that Digitek had been adulterated?
A. Yes.
Q. And when did they make that determination?
A. I think it was in 2008.
Q. April of 2008?
A. I think that's the date.
MS. DOWNIE: I don't have any further questions. Thank you. Thank you very much.
THE WITNESS: Pleasure.
FURTHER CROSS-EXAMINATION
BY MR. MORIARTY:
Q. I have four subjects I want to talk to you about. One is have you ever published anything about FDA regulations, pharmaceutical quality assurance or pharmaceutical quality control testing?
A. I think we encourage people to report those in the FDA Med Watches in a

publication that we had at The Drug & Poison Center sometime ago.

Q. Is that it?

A. Yeah, I think so.

Q. Let me make sure I understand this increasing incidence of toxicity above two nanograms per milliliter. If I understand what you're saying, above two there's an increasing chance of toxicity, correct?

A. Yes. It does increase as the serum level goes up.

Q. Is there a level or do you know at what level it is more likely than not that someone will have clinical toxicity?

A. Well, it's fifty percent. You can look at the level that gives you fifty percent arrhythmias and that will answer your question.

Q. Well, I'm looking at the chart you have pulled out for Goodman & Gilman and it says concentrations -- and I'm distilling these out and you can look at it if you think I'm reading it wrong -- concentrations of 1.7 are associated with a ten percent probability of digoxin-induced arrhythmias. Concentrations of 2.5 would be associated with fifty percent

probability of digoxin-induced arrhythmias. And then concentrations of 3.3 associated with ninety percent probability of digoxin-induced arrhythmias. Is that what this is saying?

A. Yes.

Q. And that's according to these two references in 1970 and 1988, correct?

A. Yes.

Q. Obviously there's other PK data regarding digoxin other than those two things, right?

A. Oh, yes, there's hundreds of papers.

Q. So the -- but just based on those studies and Goodman & Gilman, it's a fifty percent probability at 2.5, correct?

A. Yes. Half the people are going to have it.

Q. Now, help me make sure that I'm reading this correctly. Do you mind if I come over there?

A. No, not at all.

Q. It's very small print.

A. It is.

Q. You see here in the final column

under the peak concentration banner, it says NT, does it not?

A. It does.

Q. And NT according to the thing down here is not -- no signs of digitalis toxicity right here by my finger. You see that?

A. Yes.

Q. And then T would be --

A. Toxicity.

Q. -- toxicity?

A. Right.

Q. So what they are saying is NT 1.4 nanograms per milliliter plus or minus point seven?

A. Yes.

Q. Is that correct?

A. Yes.

Q. And toxic --

A. Goes all the way up to 2.1.

Q. And toxic is 3.7 --

A. Um-hum.

Q. -- plus or minus one --

A. Um-hum.

Q. -- correct --

A. Yeah.

Q. -- according to Gilman & Goodman?
A. Yes.
Q. Okay. The last thing I want to ask you about is the null hypothesis.
A. Yeah.
Q. I was asking you before about FDA regs and who needs to prove and give assurances about the safety of tablets, et cetera, and you mentioned the null hypothesis. Tell me why you mentioned the null hypothesis in that context.
A. Well, the null hypothesis is the basic assumption of science that something is not true unless and until you prove it. When you're dealing with pharmaceuticals and you cannot prove the concentration in a tablet, we don't use the null hypothesis to decide whether that ought to be given to patients. What we use is that reasonable quality control has been applied. It's a different set of assumptions than the null hypothesis, and the reason is that the consequences of being wrong are tremendous.
Q. You're talking about the regulatory public health side, correct?
A. I'm talking about the

responsibilities that we have as manufacturers to physicians, pharmacists and patients. The responsibility is that we can prove to a reasonable extent, point oh five, whatever you want to use, the usual assumptions that that product contains what we say it contains, and if we can't, we assume that it isn't rather than we assume, oh, it's okay, let's give it to patients.

Q. When was the last time you personally were involved in the manufacturing of pharmaceutical solid oral dose forms?

A. Let's see, solid oral dose forms. Boy oh boy oh boy. I made some while I was in school and that would be in the '60s, the '70s. And I made some liquid preparations in the 1980s.

Q. When you were making the tablets in the '60s or '70s, they weren't for mass produced sale to the public, were they?

A. No, they were not.

MR. MORIARTY: All right. I don't have anything else. You have anything else?

MS. DOWNIE: No, thank you.

MR. MORIARTY: You can explain

waiver. You're not going to ask questions, are you?

MR. THOMPSON: I'll reserve my questions for another time. Dr. Nelson, you have given many depositions so you know you have the right to sign the deposition. You also have the right to waive it. So as much as I hate to say this, I think that you ought to have an opportunity to read it and sign it. So, Madam Court Reporter, I'm happy to coordinate that with you to save you the trouble and if I screw it up, then it becomes final anyway without a signature so I would like to do that.

(Thereupon, the deposition was concluded at 12:41 p.m.)

I, EJORN D. NELSON, PHARM.D., do hereby certify that the foregoing is a true and accurate transcription of my testimony.

_ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Dated _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

STATE OF OHIO)
COUNTY OF MONTGOMERY) SS: CERTIFICATE

I, Mary Jo Stevens, a Notary Public within and for the State of Ohio, duly commissioned and qualified,

DO HEREBY CERTIFY that the above-named EJORN D. NELSON, PHARM.D., was by me first duly sworn to testify the truth, the whole truth and nothing but the truth.

Said testimony was reduced to writing by me stenographically in the presence of the witness and thereafter reduced to typewriting.

I FURTHER CERTIFY that I am not a relative or Attorney of either party, in any manner interested in the event of this action, nor am I, or the court reporting firm with which I am affiliated, under a contract as defined in Civil Rule 28(D).

IN WITNESS WHEREOF, I have hereunto set my hand and seal of office at Dayton, Ohio, on this _ _ _ _ day of _ _ _ _ _ _ _ _, 2010.

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MARY JO STEVENS
NOTARY PUBLIC, STATE OF OHIO
My commission expires 9-10-2011